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THE PINEAL GLAND, ESPECIALLY IN RELATION TO THE PROBLEM ON ITS SUPPOSED SIGNIFICANCE IN SEXUAL DEVELOPMENT

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The pineal gland, glandula pinealis, corpus pineale, epiphysis cerebri or conarium is an organ, the function of which has remained unknown up to the present day. Correlated with this lack of knowledge is the fact that the organ has been the subject of the most various theories. During a philosophical and speculative period this centrally situated organ was considered to be the seat of central psychic activity. At a later period, the "acervulus cerebri" contained within the organ, which apparently always attracted attention, was for this reason considered as very important. Later, it was learned that this organ is homologous with the pineal eye in lower forms and it was relegated to the status of a rudimentary organ without any significance at all. Still later, the observation of a connection between tumors in the pineal gland and precocious development in the genital sphere opened the eyes of authors to the possibility of the pineals being an incretory gland and various observers who performed experiments upon animals have, in the opinion of many, supported this hypothesis. In a period in which the study of the internal secretions has seen, more than ever, days of full bloom, many technical faults have been committed in the investigations. In the studies on the pineal gland, one has very

often the impression that the authors' desire to consider the organ as incretory in function is greater than their critical judgment regarding published researches. There is a priori no justification for entertaining such a desire or even the opposite.

In the following pages, I shall give a report of our present knowledge of the pineal gland and show what conclusions as to its function may justifiably be inferred. In each aspect of the problem we shall try to evaluate the arguments pro and con. Although I must confess at once that I do not share the prevailing opinion, though it may possibly be true, that the pineal gland exerts an influence on sexual development, I consider it sufficiently demonstrated that in most mammals, including man, the pineal gland is not at all rudimentary, but that it probably has an incretory function. Finally, it seems probable that future investigations will result in technique more fruitful than special study of the relations of the pineal to sexual development. It is to be hoped that investigations of its relations to the cerebro-spinal fluid and to brain metabolism will receive more adequate study than heretofore.

COMPARATIVE ANATOMY

In Inferior Vertebrates and Birds

Details as regards these groups may be found in the monographs of Studnicka and of Tilney and Warren. We may only mention that while the pineal gland has not been found in the lowest vertebrate, the amphioxus lanceolatus, it has been demonstrated, with some exceptions (as in crocodiles and edentates), in all vertebrates that have been examined from the lamprey up to the man. In the lamprey, it is a structure resembling an eye. In the higher fishes it is a sacciform structure, the walls of which sometimes resemble glands. In the urodelian batracians, the pineal gland is a simple pouch; in the anurodeles the distal part bears analogy to an eye situated beneath the skin, but the proximal part resembles a gland. In reptiles the gland is sometimes sacciform, sometimes analogous to a gland in its structure, chiefly in snakes, whose type comes near to the mammals. In birds, the organ is formed by a group of isolated follicles. Altogether the organ in the vertebrates varies from an eye-like formation to a gland-like element.

In front of the pineal gland, there exists in quite a number

of inferior vertebrates another element, the parietal eye, which is already found in the lamprey and which, in the saurians, is developed into a typical eye-like formation. In the superior vertebrates, this organ disappears or is rudimentary.

Comparative Embryology and Anatomy in Mammals

For details the reader is referred to two previous articles which I have written upon the same subject (63, 64). On the whole, the pineal gland shows, during fetal life as well as during the period of youth, a constantly progressive and augmentative development which, at the same time, implies a differentiation. It is only in the edentates that the pineal gland totally disappears; in whales it is rudimentary and in the manatees it may possibly be absent, but in all other mammals that have been investigated it presents such a characteristic development that it seems absolutely unjustifiable to call it a rudimentary organ. In the rodents, during fetal life, the exterior form is tube-like; in the adult rodents it has the form of a club or of a thread. In the most of other mammals, the pineal gland, during fetal life, has the form of a pouch or of a button; in the adults it has generally the form of a pea or of a bean. In some (rabbits and swine) the follicular structure exists in fetal life, during a transitional period, but it disappears again; it is only in the inferior mammals, didelphys, and in the elephants, that follicles are found in the walls in the adults. In full-grown mammals the organ is principally formed of a uniformly constructed parenchyma, whose main mass is formed of a specific cell-type; among the pineal cells, proper, exists a small quantity of neuroglia cells, in the superior apes (as also in the man), there are also nerve cells. In most mammals there are found an abundant quantity of nerve fibres. In the horse, swine (and also in man) we find a connective stroma in the parenchyma. In old horses and oxen there are sometimes to be found calcareous concretions. Ordinarily the organ is very vascular; this is especially true in some classes of seals. Pigment exists abundantly in the ass.

Structure of the Pineal Gland in Man

In the course of fetal life, the organ develops from two anlagen, a sacciform one and another in form of a button; at a later period they coalesce. In children and adults, the pineal gland consists of parenchyma and of trabeculae of connective

tissue. In the parenchyma, the pineal cells form the main mass and assume peculiar conditions in adults. There are seen numerous amitotic cell division and a great number of processes of "nucleus excretion." Neuroglia cells are found in a number corresponding to that observed in other parts of the central nervous system. Nerve cells are seen in larger quantities than in any other mammal; they send offshoots which end in dense bundles of button-like swellings. [However, some authors (57) do not admit the existence of nerve cells.] The partitions of connective tissue develop in the first year of life and increase in number in after-life. Nevertheless, we may find in old people connective tissue conspicuous by its scarcity and a large quantity of parenchyma is always preserved into advanced age.

After the age of 8 years (very seldom before) there exists a more or less large proportion of calcareous deposits, and oftentimes small cysts. In the connective tissue, quite a number of *mastzellen* and of scavenger cells are to be found.

What Conclusions About the Function of the Pineal Gland Can We Draw from the Anatomical Conditions of the Organ?

It must be considered as very probable that the pineal gland, in man and in most mammals, is not a rudimentary organ; the term meaning an organ which, in an earlier phylogenetic stage, had a function, but which, at the present time, is without function, the organ retaining the form of the previous stages, but now composed of indifferent supporting tissue (connective tissue, cartilage, fibrillar neuroglia). The pineal gland can then be considered as rudimentary only in the edentates, the whales and possibly the manatee. In the opossums and elephants, it must be considered as scarcely developed, but not rudimentary in the true sense of the word. The arguments in favor of the opinion that the pineal gland is not rudimentary in most mammals are the following. From first stages of fetal life until youth, the pineal gland undergoes an increase in size. It is formed of a specific and much differentiated tissue. It is very vascular. In its structure, the pineal gland usually differs considerably from the gland of a few mammals in which it is rudimentary. The conditions which have been taken as indicating its rudimentary state are the following. (1) The organ at a previous stage of the phylogenetic development has probably been an eye. But this proves nothing; it proves at most that the peripheral part

of the organ can be considered as rudimentary. With reference to the central part, there can be only a question of discontinuance of its function, but not of its rudimentary state. (2) There are found certain concretions. These deposits are also found in the membranes of the brain, but without these being necessarily considered as rudimentary organs. (3) Plates of neuroglia are found in man. However, these cannot be viewed in the sense of a destruction of tissue, but as remnants of the diverticulum which exists in fetal life.

As to the function in mammals, it is not impossible that there can exist some variations. Thus it is a striking fact that in the majority of ungulates the organ has the hardness of cartilage and is chiefly formed of fibrillar neuroglia. It is also possible that this condition may be the expression of a beginning rudimentary state. The considerable vascularization in the seals is also a variation which could indicate peculiarities in the function. Lastly, the development of the large quantity of nerve cells in man and in the higher apes is a condition which could be interpreted in the sense of an advance in the functions.

The next question to be answered is, What is the nature of that function? The first which comes into consideration is a glandular function. The arguments favoring such a function are as follows: as a whole the organ is rather like an endocrine gland; the organ is considerably vascularized; there exist numerous amitoses. Possibly the process of nucleus extrusion in man is the expression of a glandular function, but this is not at all certain. To conclude, we must remark that the glandular function has its ontogenetic analogy, because the ependyma of the choroidal plexus, which, like the pineal gland, is developed from the ependyma of the cerebral ventricles, is supposed to possess a glandular function.

If we consider, on the other hand, the arguments which could be produced against a glandular function, they center in the important objection that the protoplasm (with the exception of the hedge-hog) is extraordinarily scarce and that in mammals it does not contain granulations which ought to be considered very probably as secretory (here we except the granulations which in man are evacuated from the nuclei into the protoplasm). Nevertheless, this is not a definite proof against a secretory activity. On the contrary, that could probably indi-

cate the possibility that, in an eventual secretory activity, we have to do not with a secretion of albuminous or lipoid substances, but rather with a secretion of salts and eventually with a regulation of the concentration of hydrogen-ions or with similar processes. The presence of a large quantity of nerve cells in man does not speak against the secretory activity, because we observe quite the same phenomenon in the medullary portion of the adrenals. At the most, that could be the manifestation of the fact that, in man, there is an advance in function which is not already completely accomplished and which is in being. It is only in ungulates that it must be considered as doubtful if there really exists any secretory function, because the organ has wandered far away from the glandular type and consists chiefly of fibrillar neuroglia.

Must this (eventually secretory) function be supposed to last throughout the entire life? The answer to this question must be decisively affirmative. In an advanced age we see, it is true, some atrophy of the organ, but not more than in the other organs. There can be no question of any suppression of the function in man after puberty because, after this period, a predominant quantity of specific tissue remains in the pineal as contradistinguished from what it does, for example, in the thymus.

Could we from the histological structure draw any conclusions with reference to the nature of the eventual secretory function? The answer to that question must be negative. It will seem, beforehand, natural to admit that an organ so intimately connected with the brain and, which on all sides, is surrounded by cerebro-spinal fluid, plays a special part in the metabolism of the brain and of the cerebro-spinal fluid. This is also an hypothesis for the sake of investigation which ought to be considered more than it has been hitherto the case. But we do not have any proof that the conditions are really such.

Could we perhaps draw any conclusions from the rudimentary or undeveloped state of the organ in certain animals (edentates, whales, possibly manatee and, partly, elephants)? There are also many difficulties. In these animals, one will find such a considerable reduction in the organs (teeth, hair, genital organs) in so many and such different locations and in no lesser degree in the entire brain, that one must view this reduction of

the pineal gland only as a link in the general reduction. Farther, one must consider the possibility that in these animals another organ could have taken up the function of the pineal gland [cf. the demonstration by Broman (297) of an endocrine gland in the snout of the dasypus].

If we do not take into consideration the possible significance of the fact that it is proved that the organ has disappeared in these animals or is considerably reduced, one must be very cautious in drawing conclusions from the size of an organ as to the importance of its function. For instance, the pineal gland is relatively large in sheep, but is formed chiefly of fibrillar neuroglia. If we suppose that the eventual secretory function is connected with the pineal cells we should infer that the gland has a far more important function in carnivora, whose pineal gland is small, but consists chiefly only of pineal cells, than in sheep, in which that gland is large. However, many authors have in a faulty manner reversed the conclusion.

PATHOLOGICAL ANATOMY

The pathological changes which are the most frequently described in the pineal gland of man are tumors, which take up the site of the gland, and, in some cases, in such manner that the tumor has completely destroyed the pineal gland, and in other cases, a portion of the tissue is preserved either as a delicate coating around the tumor or in form of normal, slightly modified, pineal tissue as basis for the neoplasm.

The nature of the tumors has been various. In about the half of the cases they were sarcomata. Some of the cases have been gliomata. The denomination of carcinoma for some of the tumors is unjustifiable. That applies also to a case which has been described as an adenoma. About one-fourth of the described tumors were teratomata. This condition presents great interest, as it is striking that a tumor so rare as teratoma grows in so large a percentage in the pineal gland.

The presence of teratomata in the pineal gland can best be explained as a precocious development in fetal life. During the course of intra-uterine life, the germ of the gland, in man and in many other higher animals, comes very near the surface, nearer than any other part of the brain; for this reason, there are, to a superlative degree, conditions facilitating penetration of the elements of foreign tissue into the organ and, in that

manner, forming the starting point for these peculiar tumor formations. The incidence of teratomata is to be easily explained in this way. Nicolas and Dimitrova found in the oxen transversely striated musculature in the distal part of the pineal gland. This apparent freak, the presence of isolated muscular bundles in a part where it is difficult to assign them any function, must probably be explained in a corresponding manner as being the penetration of tissue coming from the surface. The same will apply also to the tumor described by Pappenheimer, in which quite a number of muscular fibres did exist. In a single case (Askanazy) which presents the structure of a chorioepithelioma, one must assume that the chorionic epithelium has been, in an analogous manner, drawn into the organ. However, other authors deny that the tumor was a real chorioepithelioma.

Among other tumors which present a special interest, we may mention Ogle's case of melanosarcoma in the pineal gland.

In quite a number of cases termed psammosarcomata, a number of corpora arenacea has been found. That must be viewed in natural relationship to the fact that corpora arenacea are found not only in the pineal gland, but also in the membranes of the brain; thus it cannot be brought forward as a proof that the tumor arises precisely from the specific tissue of the pineal gland.

Metastatic tumors have been found twice (Förster, Jacobi); these were a carcinoma and a sarcoma. Other pathological conditions different from tumors have been rarely described. Total absence of the pineal gland in man has been mentioned by some authors, but it cannot be considered as quite established, because when the brain is taken away from the cranium, the pineal gland becomes oftentimes detached, as the organ remains hanging by the vena magna Galeni; it is very probable that such has been the case in the reported instances of absence of the gland. I was afforded the opportunity of investigating a case in which there seemed to exist a total absence of the pineal gland. The case was that of a female infant, one year old, with considerable hydrocephalus. Serial sections through the region of pineal gland showed that the organ was transformed into a pouch of neuroglia with thin walls, without any sign of pineal cells. The infant did not present any remarkable symptoms except its hydrocephalus and, especially, no precocious puberty occurred.

The formation of cysts has been described sometimes. As mentioned above, there normally exist small cysts in the pineal gland and their size can vary in marked degree. I have myself seen twice, as casual post-mortem findings, cysts of the pineal gland. It seems that they did not cause any symptom. A single case of symptom-producing cyst is described in the literature; the cyst by its pressure has flattened the aqueduct of Sylvius. But it seems rather that this case was one of tumor with cystic formation.

Lord describes a case of syphilitic enlargement; however, there is no decisive proof that this process was really of syphilitic nature. In Pontoppidan's case, it was doubtful whether the tumor was a round-cell sarcoma or a gumma. Besides, the syphilitic process may of course invade the pineal gland as well as the other organs. I observed an example of this kind (and later did Josephy) in dementia paralytica, where the walls of the vessels in the pineal gland as well as in the rest of the brain were infiltrated by plasma cells.

In tuberculous meningitis, also, I have seen the tuberculous process involving the pineal gland. But, for the rest, concerning all that is termed atrophy, hypertrophy, fibrous changes and cystic formation in the pineal gland, we ought to stand on the reserve, because the limits for the normal findings are particularly broad precisely in the organ we speak of.

Atrophy and sclerosis in the pineal gland are described very frequently. As mentioned before, in advanced age there appears very often a slight atrophy of the organ running parallel with the atrophic senile changes in the other organs, but these changes must not be regarded as an involution of the organ. The quantity of connective tissue may vary considerably, so that the denomination of a "cirrhosis" of the organ should be taken into consideration with all possible reserves. I have seen twice, in children, an enormous development of connective tissue; one of these was a girl, aged 12, who died of osteomyelitis, but she had not presented any remarkable symptoms; the second was a subject of tuberous sclerosis of the brain associated with precocious puberty. This case is reported in "L'Encéphale" (299).

CLINICAL SYMPTOMS RELATED TO THE PINEAL GLAND

Practically speaking, the symptoms which are found in the tumors of the pineal gland can be divided in three principal

groups: (1) General brain symptoms; (2) Symptoms from the neighboring parts of the cerebrum; (3) Dysendocrin symptoms.

On the whole, the general brain symptoms are of the same character as in other cases of cerebral tumors: headache, vertigo, drowsiness, which merges into coma, neuritis optica, which can pass on to atrophy and amaurosis, vomiting and attacks of general convulsions, coma, and finally death. The development and the course of the symptoms nevertheless in some degree depend upon the region in which the organ is situated; the growing tumor very soon produces closing of the aqueduct of Sylvius and in this way a considerable hydrocephalus internus (which is nearly always found at autopsy). For this reason, we observe, at times, a conspicuously rapid development of the symptoms and often a short course from the beginning of symptoms until death. Besides, none of aforesaid symptoms is absolutely constant; even the optic neuritis disc is absent in some cases. Considerable drowsiness is a peculiarly constant symptom and, as this phenomenon, as well as the paralysis of the ocular muscles, are predominant in the clinical picture, the differential diagnosis from lethargic encephalitis presents several difficulties.

The symptoms from neighboring organs are primarily symptoms from the nuclei of the ocular muscles and from the tracts in the corpora quadrigemina. In this category, the palsies of the ocular muscles are also very frequent symptoms. They can be attributed in part to a palsy of the abducens, which may be considered in the light of a general symptom of brain compression. However, there have been observed in a series of cases indubitable palsies of the oculo-motor and of the trochlearis without palsy of the sixth nerve. The other localized symptoms from the brain must rather be considered as distant symptoms. There has been observed palsy of the facial nerve and of the extremities, on one side or on both, hemianesthesia, hemiataxia and tremor, forced position of the head and of the eyes, nystagmus and, in some cases, deafness. As a whole, these symptoms do not present anything characteristic. The palsies of the ocular muscles have only, properly speaking, importance for the diagnosis. When they appear at an early stage of the disease and are much marked in comparison with the other symptoms from the brain, they should direct attention to a localization of a

tumor in the region of the corpora quadrigemina, *i. e.*, in the pineal gland or in its immediate vicinity.

The dysendocrine symptoms can for a considerable part be regarded as pituitary (or infundibular) symptoms. That applies very probably to the adiposity, which has been described in at least 8 cases (Marburg, Bailey and Jeliffe, Schmidt, Nothnagel, Müller, Daly, Kny, Löwenthal) and perhaps some others. Furthermore, in some cases, polyuria has been observed. Since these symptoms, as we know, are found very frequently encountered in diseases of the pituitary body (without complicating disturbance of the pineal gland) and since, in a number of cases, the pituitary body has been found flattened by the increased cerebral pressure, there is no little reason to consider these symptoms as distant pituitary symptoms and not as pineal symptoms. Whether these symptoms are due to pituitary disturbances or to deranged function of mesencephalic centers is an interesting problem, but outside the scope of this paper.

The cases in which complication with affections of other endocrine or possibly endocrine glands has been observed occupy a very remarkable situation. That applies, for instance, to the Case I of Neumann in which the thyroid gland was considerably enlarged, the thymus large and lobulated; also to the cases of Christ, in which existed a struma gelatinosa totalis and hyperplasia of the thymus, and of Raymond-Claude, in which small adenomata were found in the cortical portion of the adrenals, and to the case of Goldzieher, in which the adrenals were hyperplastic. We cannot determine of a certainty whether in these cases, we have to deal with secondary phenomena or with coincident anomalies.

Lastly, we come now to the well known cases in which there had been precocious development of secondary sex characters or of the body as a whole. In the year 1883, Henrot described a case in which there was a concomitance of acromegalic gigantism and of sarcomatous tumor both in the pituitary body and in the pineal gland. Gutzeit (1896) observed a teratoma in the pineal gland complicated with considerable development of pubic hair in a boy of 7 years and 3 months. Huebner and Oestreich-Slawyk, who have separately reported the same cases, have found in a boy of 4 years with a so-called psammosarcoma (afterwards it was recognized as a teratoma—Askanazy) in the

pineal gland, an anomalous size (108 centim.) and an anomalous body-weight (20 kg.) hypertrophic mammae with colostrum, hypertrophy of the penis, testicles the size of a dove egg, and pubic hair 1 cm. in length. At autopsy, the adrenals were found normal. In the year 1899, Ogle, besides the previously mentioned case of melanosarcoma of the pineal gland, reported a case of "alveolar sarcoma" (indubitably a teratoma) in a boy of 6 years. This patient had a large penis and abundant hair on the pubes, but the testicles did not seem increased in size. The adrenals are not mentioned. Frankl-Hochwart reported in 1909 the following case: A boy, aged 5 years and 6 months, in whose near parental relations existed numerous congenital anomalies (bronchial fissure, hemangiomata, naevi), died of a teratoma in the pineal gland. From the age of three, he had presented an extraordinary increase in height and a precocious maturity of mind. Four weeks before death there appeared a marked development of the penis, hair-growth on the genital organs and tibiae and a low-pitched voice. Bailey and Jelliffe's case of teratoma in a boy of 12 years (1911) presented, in addition to adiposity, a rapid development, but no pubertas praecox. In a boy of 16 years with a so-called angioplastic sarcoma in the pineal gland, a kind of tumor which resembles chorionepithelioma, Goldzieher found extraordinarily large genital organs, rapid growth of hair on the trunk and pigmentation of this part of the body. The adrenals were conspicuously large. The case of Takeya, in which the development of the secondary sexual characters began at the age of 15, is such that it is doubtful if it could be considered one of precocious puberty. Hijmans van den Bergh reported, in 1913, a case of teratoma in a boy of 9 years who had large testicles and a penis like that of an adult, well developed pubic hair extending to the umbilicus, and a voice like an adult. In 1915, Odermatt published a case of teratoma in the pineal gland in a boy of 10 years. This patient, at the age of 5, acquired a large penis and hair on the pubes three to four centimeters in length. At the age of 7, he had abundant hair on the pubes, pigmented nipples, hair on the extremities and a little beard. To these cases we may add some that are more dubious, as those of Pellizzi, v. d. Heide and A. Josefson, in which autopsy reports are lacking. The case of tumor in the pineal gland, in which masturbation or erections

were mentioned as the only symptoms of pubertas praecox, cannot be numbered among our cases, as these phenomena occur so frequently in normal children that we cannot attribute to them any significance.

The evidence as a whole indicates beyond doubt that there exists a relationship between the appearance of tumors in the pineal gland (nearly always teratomata) and certain phenomena of growth in the sense of an abnormally precocious development of genital organs, hair-growth, and bodily development. The question to elucidate is now: Of what nature is this relationship?

In studying the available evidence one encounters the difficulty that the evidence is deficient in many points, partly because the observers have made the autopsy only of the brain. As is known, in most cases the pubertas praecox has been found as an autonomous disease, which often leaves no sign at all after the normal period of puberty. In another class of cases, the precocious puberty, most certainly under the form of a precocious virilism when it exists in girls, has been found complicated with tumors of the cortical part of the adrenals. However, in the majority of cases of pubertas praecox with tumors of the pineal gland, exact descriptions of the adrenals are not given. Goldzieher observed large adrenals and Raymond and Claude have found a sort of adenomatous formation in the cortical portion of the adrenals, while, on the other hand, Oestreich and Slawyk found normal adrenals. Disregarding deficiencies in the evidence, the conclusions to be drawn from the coincidence of teratomata in the pineal gland and of precocious puberty, are rendered difficult, because we have six elements to take into account: (1) Secretion of substance from the tumor itself; (2) Destruction of the pineal gland; (3) Destruction of the neighboring brain centers; (4) Distant action on the hypophysis; (5) The constitutional element which expresses itself in the development of the teratoma, and (6) Deficient investigation of the other organs.

Concerning the secretion of substances from the tumor itself a series of various factors is brought into play. In none of the cases has the tumor been an adenoma or, more exactly, "pinealoma," but always a teratoma. Now the teratomata, generally speaking, never gives rise to precocious puberty. On the other hand, in the experimentally induced teratomata which

develop after injection of fetuses reduced to pulp (Starling), some authors have succeeded in accelerating pregnancy, *i. e.*, the secretion of substances from teratomata seems to have an influence upon the genital system. Furthermore, we have to take into account that the teratomata of the various regions contain different tissue elements (Starling), hence it is possible that teratomata of the pineal gland especially may contain tissue elements which produce substances, and these substances again stimulate to the development of the secondary sexual characters. Among such tissue elements in the teratomata of the pineal gland, we must principally be mindful of the cystic glandular formations, which are often described, formations which, however, seem to originate from the cylindrical ependym of the posterior commissure (organon subcommissurale), rather than from the pineal gland. The opinion that the substances produced by the teratoma itself are the cause of the pubertas praecox, of which opinion Askanazy has been the chief proponent, must certainly be taken into consideration in a higher degree than hitherto. But as teratomata must be viewed in the light of formations originating from the exterior, which invade the pineal almost as a sort of parasite, it is unjustifiable to consider them as hypersecreting pinealomata from analogy with the adenomata of the hypophysis which induce acromegaly. Furthermore, it is unjustified to reason from such pathological conditions to the normal function of the pineal gland. Besides, in the development of precocious puberty in the cases of tumors of the cortex of the adrenals, we have an analogy relative to an eventual chemical action originating from these teratomata. As I have pointed out in another place, one cannot, however, reason from that to the function of the adrenal cortex in relation to an action upon the genital development, because these tumors did not probably take their origin from the adrenals as such, but from ectopic portions of the genital anlage (298). The destruction of the pineal gland is another factor which has to be taken into account. But if we consider that this is not the only possible factor, but that, as mentioned, this phenomenon is associated with the presence of an eventually secreting tumor with influence upon the cerebral brain centers and upon certain constitutional conditions, it is unjustified to conclude, as do many others, that it is precisely the destruction of the pineal gland which

causes the pubertas praecox. Such a conclusion will be legitimate only when it has been demonstrated, in a series of cases, that an atrophy, without complications, of the pineal gland has induced precocious puberty, in the same manner as in the atrophy of the hypophysis without complications there has been observed dwarfism (nanism), which renders probable an influence of the pituitary body upon growth. Nevertheless, in a series of cases of tumors destroying the pineal gland in children, there does not exist pubertas praecox; in the same manner as in the above mentioned case of hydrocephalus in destruction of the pineal gland there also did not exist pubertas praecox.

We must take into account also the destruction of neighboring brain centers in the mesencephalon. For instance, many authors have expressed the opinion that such destruction is the cause of certain disturbances of development and metabolism in the affections of the pituitary body. But, however, all this question is, at the present day, so unsettled that it is not possible to take a definite standpoint in the problem; we must consider it as a distant possibility, a possibility which has in its favor a somewhat limited probability.

The distant action of the pineal upon the hypophysis can be left out of reckoning, since, in spite of the probable importance of the hypophysis in relation to the sexual functions, pubertas praecox has never been observed in association with affections of the hypophysis.

The constitutional element must, to a high degree, be taken into consideration as a possibility. Experience shows that in many cases of diseases in various organs we are confronted by phenomena running a parallel course and of which the one cannot be regarded as the cause of the other. We can mention, as examples, a disease such as tuberous sclerosis in which, coincident with disorganization in the brain, we find formation of tumors in the heart and in the kidneys; another example is the hepato-lenticular degeneration (Wilson's disease, pseudosclerosis), in which the affection of the liver and the degeneration of the lenticular nucleus run a parallel course; or, lastly, a series of cases of pluriglandular insufficiency, in which there exists an action upon quite a number of different endocrine glands.

In the case of complication with tumors of the pineal gland

and pubertas praecox, we must then think of the possibility that we have to do, at the same time, with an anomalous disposition of the region of the pineal gland and of the endocrine elements of the testicles. A case which could indicate a possibility in this direction is that of Goldzieher, where, in addition to the tumor of the pineal gland, existed a hyperplasia of the adrenals, which must be considered as having a relationship to the hypertrichosis. In the case of Raymond and Claude, we find also such an apparent parallelism between the tumors of the pineal gland and a formation of adenoma in the adrenal cortex. Furthermore, we must point out that in nearly all (and possibly all) described cases of tumor in the pineal gland, associated with pubertas praecox, we had to do with teratomata, that is to say, a tumor which has a marked relationship to malformations.

In the cases of teratomata of the pineal gland in which precocious puberty has developed, we have then to take into account the combination of at least three factors: secretion originating from the teratoma, destruction of the pineal gland, and general anomalous disposition of the organism. This does not preclude that the syndrome, pubertas praecox-pineal tumor, presents interest for the diagnosis. But this cannot justify inferences as to the function of the pineal gland, especially as to its significance (inhibiting or accelerating) for the development of the secondary sexual characters.

EXPERIMENTAL INVESTIGATIONS UPON THE PINEAL GLAND

As early as 1898, Howell made the first experiment of injecting extract of pineal gland. However, it was only after Marburg, in 1908, had published his large work on the pineal gland (in which he emphasized its rôle as an endocrine organ) that the experiments were started, partly as extirpation, partly as feeding experiments and injections of the extract. In large part, the experiments gave negative or contradictory results, and, in part, they lacked the necessary experimental control. On the whole, it may be said that there is always a wide field open to experimental research concerning the pineal gland.

I. Experimental Extirpation

Exner and Boese (1910) destroyed the pineal gland in about 100 young rabbits. In 6 of them, in which subsequent microscopic examination showed that the destruction had been

total and which had survived a time sufficient to judge the effect, there was not any effect upon the development of genital organs.

In the same year, Sarteschi extirpated the pineal gland in 11 rabbits; 2 of them survived the operation. There appeared retardation in growth and cachexia, which disappeared again. It seemed that the animals remained sterile.

Biedl carried out a large series of experimental extirpations on dogs. Three of them which survived the operation for a period of two months exhibited no symptoms (the three animals were, however, adult). At autopsy it was found that the pineal gland was completely absent.

In 1912, Foà tried total extirpation of the pineal gland in young rabbits, but without any result, because all animals died some days after operation. He was, however, more successful with young chickens, aged 3 to 5 weeks, as 15 of them survived the operation. In the first 2 or 3 months the animals were retarded in their growth as compared with control animals; but afterwards they presented a greater development and, in 3 of them, which were cocks, there appeared a more rapid growth of the testicles and of the secondary sexual characters. Eight to eleven months after the operation there existed a considerable hypertrophy of the testicles and of the combs. The operation was without any effect on the weight of the thymus. With the exception of the retardation of growth during the first months, changes could not be observed in hens; they began to lay eggs at the normal time and the crests did not show hypertrophy. In a series of control animals, corresponding changes could not be ascertained.

In 1912, Christea extirpated the pineal in 30 young cocks; 12 of them survived for a considerable period. The animals which were operated upon presented a marked retardation in development of the genital characters, as comb, spurs, and voice; also the growth of feathers was retarded as compared with that of control animals. The development of the body was not particularly delayed. The animals were rather apathetic. Marked atrophy of the testicles was noted.

Sarteschi published in 1915 a series of new investigations: he performed pineal extirpation on several rabbits and on very young dogs. In the male animals which survived the operation, he found a considerable hypertrophy of the testicles and, in one

of them, he observed, in addition, an important increase in weight and obesity (a thing which Foà did not observe in his chickens). The results in the female animals could not be judged.

Foà, in 1914, also reported new experiments. Of 10 chickens which were operated upon, 7 survived; 5 were hens. The experiments confirmed the earlier results; at first, there was a slight diminution of weight, and afterwards, in the young cocks, appeared hypertrophy of the comb and of the testicles. No corresponding changes supervened in the hens. Microscopic examination of the endocrine glands did not show any abnormality, except changes in the testicles. The canals were wider in the experimental animals. Furthermore, Foà undertook experimental extirpation in 8 young rats, 4 of which survived the operation. On one of these, a female, there did not appear any noteworthy manifestation; in three males, the somatic development attained its maximum more rapidly, but the differences were very soon abolished.

L. Adler, who is right in pointing out that we must expect different symptoms of suppression after pinealectomy in the different animal species, tried, in the year 1914, to destroy by thermocauterization the pineal gland in tadpoles. Out of 350 animals treated in this manner, 100 survived four days. Eight days after, 30 animals were still alive and they were the same size as the controls. After another week, 9 animals were still alive, and in these, during the following period, the development was very irregular by comparison with the control animals. Later on, the majority developed edema, of which they died. There was not any abnormality in the sexual development. The author states that the irregularity of development must be ascribed to the disturbances induced by the pinealectomy in the whole of the endocrine system.

In 1915, Dandy published the results of pinealectomy in dogs. After some negative experiments he developed a technic by which the organ was extirpated from in front, a notch in the posterior portion of the corpus callosum having previously been made. The operation was performed on young puppies, whose ages varied between 10 days and 3 weeks and at the same time on some full-grown dogs. The animals survived the operation for a period averaging from 3 to 15 months. None of the animals operated upon exhibited any change in development or in

psychic condition. Especially, there was not any sexual precocity, nor any abnormality in the sexual organs. The microscopic examination of the endocrine glands did not reveal any change in these. The author concludes that the pineal gland is not necessary for life and does not seem to have any influence upon sexual development.

Horrax (1916) tried, without success, to extirpate the gland in dogs, cats and young rabbits. But extirpation was quite successfully performed in guinea-pigs. Forty-eight of the young animals, in which the operation was successful, lived to sexual maturity or until they were sacrificed. In 15 male animals and in 20 females, the microscopic examination (sections in series) of the brain revealed that the pineal gland has been extirpated *in toto*. The females did not exhibit any difference in the development of genital organs in the operated animals and in the controls. Three of the female guinea-pigs became pregnant, but aborted. The following conditions were found in the male animals: there was not any difference in weight between them and the control animals; but, on the other hand, the testicles showed an average weight of 354 mg. in the operated animals, while they had an average weight of 663 mg. in the control animals. (But it must be said that there were large variations in the total weights and that the author did not make a calculation of the average error.) The vesiculae seminales were also enlarged and upon the microscopic examination were found more developed. There existed a marked spermatogenesis, but this phenomenon was more limited in the control animals. In rats, in which the extirpation was even more successful, the results were partly brought to nothing by an epidemic. In the few which could be examined, the increase of development in the testicles existed in only one animal; the others presented dubious results.

E. R. Hoskins and M. Hoskins have (1919) removed the pineal gland from 70 young larvae of Rana sylvatica, but it regenerated either partially or completely and the larvae grew normally.

If we sum up the evidence on experimental extirpation, the results, as a whole, are seen to be altogether negative. It seems to be established that the pineal gland neither in dogs, rabbits, guinea-pigs nor in hens, is an organ of vital importance. Furthermore, we are obliged to assume that the function of the

organ, in any case, in dogs, rabbits and guinea-pigs, can be taken up by one or more other organs in the case of a suppression. The results which most frequently are considered as decisive are those of Foà. But the results obtained by Christea are totally contradictory to those of Foà. Therefore, it is impossible at the present time, to reach a decision concerning the significance of these experiments.

Concerning Horrax's experiments we must point out that, in spite of their number and technical perfection, the variations in the weight of the testicles were so considerable, as above stated, that one cannot compare the average weights without a calculation of the average error. Yet they show the possibility of an activity of the pineal gland resembling that discovered by Foà in hens.

If we disregard the fact that these experimental results are as yet not confirmed, a question now arises: What part does the pineal gland play in hens, since, although its structure and size are the same as in cocks, experimental extirpation gave negative results? This condition indicates strongly that the action upon the development of puberty, if there really is such, is only of a subordinate and secondary nature.

In comparison with the altogether less valuable injection and feeding experiments, the experimental extirpations are unhappily very few in number, by reason of technical difficulties. It is important that these experiments be extensively repeated. Furthermore, it would be important to undertake such experiments partly on apes and partly on animals which possess a much developed organ, for example, on seals.

II. Transplantation Experiments

Exner and Boese have transplanted the pineal gland with the result that it has soon been completely resorbed.

E. R. Hoskins and M. M. Hoskins (1919) transplanted the anlage of the pineal from larvae of Rana sylvatica into 19 other young larvae. It failed to grow.

III. Action of Castration Upon the Pineal Gland

Sarteschi (1910) examined the pineal gland in various castrated rabbits and did not observe any divergences from the normal.

Biach and Hulles (1912) castrated a series of cats, aged 3-4 weeks. Of 15 animals operated upon, 7 males and 2 females survived. Microscopic examination revealed that in the castrated cats the pineal cells were further apart, and the nuclei and the cytoplasm were less abundant; the cytoplasm was darker in color, oftentimes shriveled; the entire cell had lost its rounded form and was angular. The authors think that the cause lies in an atrophic condition of the entire gland as well as the single cells, and they believe that it is the expression of a certain reciprocity. The phenomenon was seen in both male and female animals.

In contradistinction to these results, Ruggeri (1914) found that in rats, after castration, there appeared an increased number of cells and a greater uniformity of the lipoid elements as well as marked development of mitochondria.

Pellegrini (1914) has reported results contradictory to those of Biach and Hulles. (I have not been able to consult his work in original.)

Aschner (1913) examined the pineal gland in pregnant, virgin and castrated guinea-pigs, rabbits, dogs, and cats, respectively. Litter controls were used. In pregnancy, he found the gland shorter, broader and more rounded, while it was more pointed in virgin animals. In the castrated, he observed marked atrophy; that phenomenon was most conspicuous in cats. Histologically, there was in pregnant cats a slight increase of the fat-containing vacuoles which lay imbedded in the interstitial tissue, but these are not specific elements of pregnancy.

The castration experiments as well as the experimental extirpations have thus given contradictory results. We are not entitled to draw from them conclusions concerning the function of the pineal gland and particularly concerning its relationship to the genital organs.

IV. Electric Stimulation of the Pineal Gland

De Cyon (1903), in three rabbits, exposed the pineal gland, which he stimulated electrically. Even the slightest contact with the electrode induced slight changes of form in the organ, as it contracted and at the same time modified a little in its position. The author thinks that this should have been ascribed to vasomotor action, if the organ had been very vascular (as is really the case); but, as he did not recognize that, he assumed that the

pineal gland plays a mechanical part in regulating automatically the flow of cerebro-spinal fluid, through the aqueduct of Sylvius. In a way, de Cyon supported his theory by the findings of Nicolas' and Dimitrova's, who observed transversely striated muscular fibres in the pineal gland of oxen. In a later work (1907), de Cyon maintained his opinions. In a like manner, Pellegrini tried electric stimulation (I could not procure the original work). Precisely by reason of the marked vascularity of the organ, no conclusions about a mechanical function can be drawn from the electric stimulation.

V. Chemical Investigations on the Pineal Gland

Fenger collected the pineal glands from a total number of 2358 oxen, 1348 sheep and 5062 lambs. The organs were desiccated in vacuo and a benzine extract was prepared. He determined afterwards moisture, ash, phosphoric acid and total nitrogen. The glands from young animals contained less phosphorus and more total nitrogen than those of full-grown animals.

VI. Injection Experiments

In 1898, Howell injected glycerinated extract of pineal gland. The results were inconstant; in some cases there was no effect, in others the blood pressure was lowered. In any case, the action was different from the constant and characteristic reaction induced by injection of pituitary extract.

De Cyon (1903) injected into rabbits extract of pineal gland from oxen and sheep. He observed that after intravenous administration the heart beats became more frequent and irregular, but there was not any change of blood pressure. Similar, although not quite the same, results are obtained by injection of glycerophosphate of sodium or calcium; he thought, therefore, that the pineal gland influences calcium metabolism. These results seem far from convincing, in consideration of the fact (which de Cyon himself admitted) that the pineal gland often contains calcareous concretions.

Jordan and Eyster have found that intravenous injection of aqueous extract of the pineal gland from sheep produced in rabbits more marked changes of blood pressure than the corresponding extract of other parts of the brain.

Jordan and Eyster found further (1911) that the pineal gland of the sheep contains some substance which, on intra-

venous injection in certain animals, causes a fall of blood pressure associated with a vasodilatation in the intestines, produces a slight degree of improvement in the beat of the isolated cat's heart and causes a transitory diuresis associated with glycosuria in about 80 per cent of the cases. The effect on blood pressure in the cat is small and unimportant. On the whole, the action of pineal gland extracts is relatively slight when compared with that produced by extracts from other glands known to furnish internal secretions.

Dixon and Halliburton repeated the experiments of de Cyon, but found that the injection of extract had no action on heart beat, blood pressure, respiration, intestinal or urinary secretion. Furthermore, they found in later investigations that, while the extract of plexus choroideus and of brain substance injected intravenously in dogs, induced an increase in secretion of the cerebro-spinal fluid, that was not the case with the extract of pineal gland.

Ott and Scott (1910-1911) have made a series of experiments by intravenous injection of pineal extract in lactating goats. The injection had a marked galactogogue effect in the same manner as thymus, corpus luteum and pituitary extract. Preliminary intravenous injection of atropine lessened the galactogogue effect. Further, the injection produced a transitory depression of blood pressure and increase of kidney volume caused by vasodilatation. Also for the male genitalia in cats and probably the mammary gland, the pineal extract acted as a vasodilatator. Application of pineal extract to a uterine strip of a pregnant rabbit caused increased contraction. Local application of pineal extract gave pupillo-dilatation in rabbits when the superior cervical sympathetic ganglion has been excised.

Cushing (1912) obtained negative results on blood pressure and circulation with intravenous injections of the aqueous pineal extract.

Schäfer and Mackenzie (1912) investigated the action of a large number of animal extracts upon the flow of milk from the lactating mammary glands. They were not able to confirm the galactogogue effect of pineal gland extracts reported by Ott and Scott. By later investigations, Mackenzie has found that

intravenous injection of pineal extract of sheep had a slight galactogogue effect, perhaps due to absorption of a small quantity of pituitary extract from the cerebro-spinal fluid.

Dana, Berkeley, Goddard and Cornell found (1913) that by injection of pineal extract in half-grown guinea-pigs, the weight of the animals increased more than the weight of the controls. The same was found in baby guinea-pigs, rabbits and kittens; both weight, size and intelligence were augmented.

Fränkel (1914), by injection of pineal extract, obtained a distinct dilatation of the cephalic vessels and he saw in that action an opposition to the suprarenal glands.

Prior (1915) investigated, in rabbits, aged 10-35 days, the effect of injection of glycerinated extract of pineal gland of calves. Every fifth day, he injected constant quantities. Pure glycerine was injected in the control animals. Weighing and measurement of three animals and of controls showed him, contrary to the findings of Dana and Berkeley, a retardation in growth. No abnormality was found at autopsy. They thought that these results are consonant with those of the experimental extirpations of Foà.

Horrax (1916) injected in the vena saphena externa of dogs extract of pineal gland from calves and from lambs. The injection of small quantities did not produce any result. After injection of larger quantities there was, after some minutes, a sinking of the blood pressure and, corresponding to that, a diminution in the production of cerebro-spinal fluid. The result was the same either with fresh or with desiccated extract.

Fenger (1916) prepared an extract from full-grown oxen, sheep and lamb pineals; he studied its action upon the uterus musculature. The effect was less marked than was that of the anterior lobe of the hypophysis and much less marked than that of the posterior pituitary lobe. As previous experiments had shown that the effect on pulse rate and blood pressure is also problematic, the author concluded that it is difficult "to consider the pineal body as an internal secretory organ of medical value."

Bab (1916) found that injection of pineal extract had no remarkable influence on diuresis.

VII. Feeding Experiments

Dana, Berkeley, Goddard and Cornell (1913-1914) have instituted feeding experiments with pineal gland from oxen. Half-adult guinea-pigs, after being fed with pineal gland, showed a more rapid increase in weight than control animals; the same was true of kittens and rabbits. Feeding experiments in children (a boy and a girl) for three weeks gave a little augmentation of the elimination of nitrogen in the urine and, as to the rest, there was not anything noteworthy. Furthermore, they experimentally fed a number of mentally deficient children and thought some improvement in their mentality resulted. Goddard has, however, continued the above mentioned experiments; he found no amelioration after a long period of treatment. Especially, he found that the extracts were quite without effect on certain mongoloid idiots. Later (1920), Berkeley reported that the feeding of kittens, rabbits and guinea-pigs with preparations of pineal gland from calves and young cattle accelerated the somatic growth to a marked degree and that a number of backward children without organic stigmata to whom the gland was administered for a sufficient period made an advance in mental age considerably in excess of any previous progress for a like period.

Dresel (1914) found that pineal feeding (epiglandol) had no influence on the blood sugar.

Hofstätter (1917) treated 11 girls and women suffering from exaggerated sexual libido with pineal medication. In 7 cases he obtained good results. In 3 lactating women he found an augmentation of the milk secretion.

Pilez (1918) treated a case of possible dementia praecox (mania?) with epiglandol and reported some depression of the sexual excitation.

Summing up the results of experimental extirpation and of experimental feeding, we see that they give us in many points contradictory issues and also results. These by nature must be uncertain, for instance, amelioration of mentally deficient children after feeding, as these patients may often present spontaneous progress in the course of time. Besides, it is interesting to see how frequently the results of the authors seem to depend upon their preconceived idea either that the pineal gland is an

accelerating organ for development or that it is an inhibiting organ.

Setting aside this part of the question, the action of feeding or of injections of pineal gland extract cannot, in the nature of things, serve to elucidate the function of the organ. We must, for instance, remind ourselves of the fact that the pineal gland is an organ very rich in nuclein and contains, therefore, probably an abundant quantity of nucleinic acid. But in the control experiments it has not been habitually determined whether feeding with corresponding quantities of nucleinic acid induces a similar action on the growth and on the development of the individuals experimented on. Furthermore, we must remember that the pineal gland of oxen and sheep contains an abundant quantity of neuroglia fibers. Feeding with neuroglic tissue from other parts of the central nervous system should thus be considered as a necessary control experiment. All tissues, including the pineal gland, are formed of various substances which are indispensable to the building up of the tissues themselves; but these substances are not an expression of the specific function of the tissues. One ought not to be astonished if many of those substances can produce, by injection or by feeding, alteration of form or function. And as long as these substances are not excluded, most conclusions from experimental feeding or injections must be considered as unjustified.

CONCLUSIONS AND FINAL CONSIDERATIONS

In the present stage of experimental study, our knowledge of the *constitution of the pineal gland* in vertebrates and also in the man has the same extent as our knowledge of the constitution of the other organs of the body.

Our knowledge of the *clinical results of pineal gland tumors* has been enriched, chiefly by the works of Marburg and Frankl-Hochwart, so that we recognize a clinical picture, in which pubertas praecox coincides with teratoma formation in the pineal gland. Thus we may be permitted in a number of brain tumors in children to diagnosticate with a great certainty that the tumor is a teratoma of the pineal gland.

But our knowledge of the *function of the pineal gland* must unhappily be considered as very defective. We can admit of a certainty that this organ has a function in man and in the

majority of mammals. We can further admit as an important possibility that this function is partly an internal secretion, but an internal secretion which is not indispensable to life. Finally, we must confess our total lack of knowledge of the influence of this internal secretion in the body and, particularly, we must point out that the hypothesis that the secretion plays a rôle in the development of puberty is, to date, completely without significant evidence.

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ADDENDUM

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THE PREVENTION OF EXOPHTHALMIC GOITER

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It must be confessed that there is a relative deficiency of interest in the study of the prophylaxis and cure of Graves' disease. Comparatively few medical men can manage to a successful issue a case of this affection, much less an attempt at prophylaxis. That is why operation is resorted to,—not because Graves' disease is medically incurable, but because there are few physicians who make sufficient sacrifices of time and energy to be able to demonstrate perfect non-surgical results. Meanwhile, thyroidectomy is performed upon thousands of these patients, "for better or for worse." If the medical profession were to become half as serious in the prevention and cure of Graves' disease as they are in tuberculosis, not only would many cases of the disease be averted, but surgeons, satisfied that internists can demonstrate excellent results, would refuse to operate on these patients.

A discussion of the prophylaxis of exophthalmic goiter (the rather inappropriate synonym of Graves' disease) does not embrace a consideration of the prophylaxis of simple goiter and of hyperthyroidism. Simple goiter is local, while Graves' disease is a generalized condition. Hyperthyroidism can be produced by the ingestion of thyroid extract; Graves' disease cannot be so produced; and though the syndrome of Graves' disease presents evidences of thyrotoxemia, there are likewise evidences of dysfunction of the entire chain of endocrine organs and of the vegetative nervous system. Attempts at prophylaxis by the administration of iodine and of thyroid extract are useful in simple goiter; these drugs are not only useless, but hazardous in Graves' disease. Moreover, the use of certain tests to assist in diagnosis of Graves' disease, depending for their usefulness on the flaring up of a dormant syndrome or an aggravation of existing symptoms, cannot be too strongly deprecated as dangerous. The reasons for this are too obvious to be enumerated.

PROBABLE ETIOLOGY OF GRAVES' DISEASE

The study of prevention of any disease must begin with an investigation of its etiology. While in Graves' disease we do not know of any specific cause or causes lending precision to our task, we are cognizant of a series of etiological influences which, if at least partly eradicated, would mean much to the world at large. We know that: (1) hereditary influences play an important part in susceptibility to the disease, as evidenced among other things by the multiplicity of cases in the same family; (2) that this hereditary predisposition may become intensified by acquired factors through errors in the conduct of life or through maladaptation to the world at large; and (3) that in nearly every case of Graves' disease there was superimposed upon predisposition an exciting factor accounting for the onset of the syndrome. We might tabulate the probable etiology of Graves' disease as follows.

A. Inherited predisposing factors.*
   1. Autonomic imbalance.
   2. Endocrine imbalance.
   3. Reduction of threshold of nervous and emotional reaction.
   4. Vasomotor ataxia.

B. Acquired predisposing factors.
   1. During infancy.
      (a) Faulty hygiene, diet and discipline.
      (b) Accidents, as falls, burns, fright, etc.
   2. During childhood.
      (a) As in infancy.
      (b) Faulty school life; impressions from companions, teachers; overambition.
      (c) Unhealthy influences of home life; table talk, parental behavior, and other home circumstances.
      (d) Improper recreation; movies, theaters, reading, etc.
   3. During puberty and adolescence.
      (a) Faulty school life as in childhood.
      (b) Faulty impressions from home environments, relatives, companions.

*The inherited predisposing factors are interrelated and inseparable.

(c) Improper recreations: movies, theaters, dancing, reading, etc.
(d) Inappropriate preparation for adult tasks of life.
(e) Harmful dietetic and hygienic habits.
(f) Changes incident to growth and development.
i. Physical-thyro-gonadal hyperplasia, menstruation.
ii. Instability of mental activity and aberrant assertion of sexual instincts.

4. During adult life.
(a) Faulty dietary habits.
(b) Harmful occupational, business, or professional factors; overactivity or inactivity.
(c) Improper sleep—quality, quantity, and regularity.
(d) Errors in social and sexual life.
(e) Faulty mental habits—pessimism, worriment, etc.
(f) Errors in quality and quantity of recreation.

C. Exciting causes.
1. Physical.
(a) Focal infections in tonsils, sinuses, teeth, gastrointestinal and genitourinary tracts, etc.
(b) General or systemic infections, especially tuberculosis, syphilis, and rheumatic fever.
(c) Autointoxications—intestinal, renal, biliary.
(d) Neoplasms, especially of pelvis.
(e) Occupational—extreme physical exertion, hazardous occupations associated with danger to life and limb, exposure to extremes of temperature and to poisons.
(f) Accidents—railroad, automobile, conflagrations, earthquake, etc.

2. Mental—Psychic trauma (either acute or sustained).
(a) Occupational—occupations entailing extreme nervous strain, *e. g.*, school teaching, telephone operating; those entailing duties at variance

with the desires of the individual, resulting in continuous distress.

(b) Economical—maladjustment between income and expenditure, extravagant habits, bankruptcy, etc.

(c) Social—"high life" and its ambitions; discord with relatives and friends, misplaced love, hatred, jealousy, and other passions.

(d) Sexual,

i. Men—sexual neurasthenia, impotence, priapism, etc.

ii. Women—vaginismus, sterility, sexual incompatibility, frequent pregnancies.

(e) Intense emotional strain—sorrow, anger, chagrin, distress, prolonged engagements.

(f) Accidents—acute fright, shock, etc., with or without physical injury.

PROPHYLAXIS OF PREDISPOSING FACTORS

What are the precise inherited influences is still uncertain, and to speak of the various theories advanced would entail a duplication of the already voluminous literature. The fact is, however, that subjects of Graves' disease are nearly always spoken of by their parents as having been nervous and delicate during infancy; their childhood was replete with persistent nervousness and semi-emotional outbreaks. There was seldom any complaint regarding progress at school; on the contrary, school work was never a task mentally, though evidently physically fatiguing. Precosity of mind at the expense of physical vitality is frequently described as characterizing school life, though most often these subjects present a floridity of the skin, indicating apparent good health.

So far as I am able to determine in my experience with a large series of subjects of this sort, the earmarks characterizing a young adult possessed of susceptibility to Graves' disease are the following. (1) *Heightened cerebration* is characteristic. Irrespective of the amount of schooling obtained, the ambitions and mental alertness of these persons are beyond those of the average individual of similar station in life. There is frequently a fondness for classical music, a surprising appreciation of the

other aesthetic arts, a desire for psychological pursuits and adventures into the realms of the occult, a craving for literature and lectures apparently beyond the mental reach of the subject; in the professions, an aptitude to reach ahead of contemporaries; in business, ambitions worthy of a captain of industry. It is from this class of individuals that many a talented person or genius arises, if the mental activities are well applied; if not, such a person may become an incipient or an actual case of dementia praecox. Occasionally the mental status is somewhat uncertain; conversation upon a topic, though intense and earnest, is unsustained, interest flitting from one subject to another with irrelevant sequence and frequency, bespeaking a veritable frenzy to acquire an encyclopaedia of information within a brief while,—an ambition never satisfied, burning away the energies day after day, to say nothing of the nocturnal activities of the subconscious during attempts at sleep. (2) *Emotional instability* brings about high spirits alternating with moodiness, laughter with tears, and not infrequently intense love with hatred. A happy medium—a stability of feelings and emotions—a degree of the phlegmatic in temperament—these are conspicuously lacking. (3) *Excitable heart and labile pulse* is seen. These subjects are apt to present heart hurry on the slightest physical or mental provocation, with or without palpitation and an "out of breath" feeling. Occasionally, the heart rate is perpetually at a figure somewhat above normal, a characteristic of which the patient is rarely cognizant; but usually the normal rate obtains during repose. The pulse is soft, compressible, and often dicrotic, and frequently indicates a status of sinus arrhythmia. (4) *Vasomotor ataxia* is evidenced by the capillary pulse, dermographia, the tendency toward hyperidrosis, and sensations of undue heat of the surface of the body, even in cold weather. (5) *The eyes are brilliant or sparkling,* especially during conversation and active attention, when there may be observed at times even a suspicion of exophthalmos. In many instances an imperfect or larval von Graefe's sign may be elicited. (6) An unusually *palpable thyroid gland* is almost constant in these subjects, though on inspection the thyroid area may appear somewhat full or even normal.

These persons are to be found everywhere—more especially among Caucasians, whose mentality is at the highest state of

development; in all strata of society, rich and poor, male and female, young and old; in all countries; and in almost all climes. While the greatest number may be combed out from the vast multitude of high school and college students, school teachers, stenographers, young business and professional men, real and would-be stock brokers; the young newlywed, the mill hand, the newsboy, and the laborer are not immune. All these are members of a community of mortals who have many things in common, physically and mentally; a generalized instability of the autonomic nervous system and of the chain of endocrine organs; a lowered threshold of emotional and reflex activity; and an ever present danger of the development of an attack of the Basedowian syndrome.

All such persons, especially if presenting a significant history, should be regarded as pre-Graves' disease patients, the object of prophylactic measures. Prophylaxis should consist of endeavors so to plan the individual's attitude and conduct with relation to the world at large as to fortify the bodily forces against Graves' disease. Presented with the opportunity of a free hand in the management of a young person born into a Graves' disease family, what can prophylaxis do to reduce or eradicate this susceptibility? The answer is obviously to avoid or circumvent the acquired predisposing factors above enumerated. The task is a difficult one; guidance must be perpetual, at least up to well established adult life; but if the task is done to within fifty per cent of perfection, the incidence of Graves' disease would probably be reduced by seventy-five per cent of the existing figure.

Acquired predisposing influences are traceable to most of the acts of body and mind of the individual. Born with a standard of physical and mental health at variance with that of his fellows, such a person will not find himself at an equilibrium with those circumstances in life which ordinarily are in entire agreement with the average person. These acquired predisposing factors occur from the very moment of birth and may continue on throughout existence, and unless the maladjustment is corrected through the interference of favorable influences, the persistence of this handicap may mean an attack of Graves' disease.

Every physician knows that an infant is rarely brought up

in an ideal way, *i. e.*, with perfect hygienic, dietetic, and mental management. Nearly always there is a varying degree of error from apparently unimportant trifles to gross carelessness which makes us wonder how the infant can survive the "fond" parents' care. Now, if one or both parents happen to be susceptible to, suffering with, or recovering from Graves' disease, we have in the offspring an instance in which hygienic, dietetic, and mental care *must* approach the ideal. To permit the baby to "just grow" is to invite a strong predisposition or inflammability to Graves' disease. For safety's sake, such children should be regarded as pre-Graves' disease subjects and, as such, the object of prophylaxis from the very beginning. The most important suggestion to parents should be the matter of not accustoming the child to flesh food. Parents are apt to consider flesh food as necessary to the attainment of growth and strength, and may begin administering steaks, chops, and the like at the early age of twelve or eighteen months. This is the first gross and most important error that could be committed.

When school life is begun, other factors become operative. Mental impressions from teachers, classmates, companions, relatives, and even parents may diminish or increase susceptibility to the disease, depending upon whether they approach or recede from the ideal. The quality and frequency of indulgence in recreation, whether at home, out of doors, or in assemblies at theaters, halls, and the like, play their part with a potentiality that is not sufficiently appreciated. The "movies" are a most powerful factor in molding the mental health and character of young America.

During puberty and adolescence, added recreational factors arise, in that the contact with the opposite sex tends to increase the existing emotionalism and mental disquietude almost, and at times, to the point of irrationality. In this category may be mentioned parlor games, inappropriate stage performances, and dance halls. An attempt must be made tactfully to avert these errors. Overambition in school and college duties and in the preparation of a career should likewise be under control. Females with a predisposition to Graves' disease must obtain complete physical and mental repose during the menstrual period, since menstruation is interrelated with the neuro-endocrine system, which latter is in a state of varying degree of

excitability at this time. Irritability, hot flushes, weakness, emotionalism, outbursts of hysteria and temper are commonly seen prior to and during menstruation. Also, at this time, a distinct temporary hyperplasia of the thyroid gland with unmistakable though mild evidences of Graves' disease, may assert themselves. In girls and young women engaged in active pursuits, this bit of advice may be difficult to follow; but when regarded in the light of serious future events, a mutual understanding on this subject is usually reached without much ado.

It is during early adult life that the greatest peril exists in persons predisposed to Graves' disease, in that faulty dietary, social, sexual, vocational and other factors may intensify susceptibility to the utmost. Dietary and related habits which tend toward an increased intake of toxins (and here the habit of constipation may be included), place a great strain upon the detoxicating mechanisms of which the endocrine organs, especially the thyroid, are a part. These patients are often passionately fond of meats, frequently taking large quantities more than once daily. This habit may be discouraged by an intimate conversation with the subject, with an explanation of the why and wherefore. I am frequently told by patients suffering with the disease that unless they take three, four or more cups of coffee daily, they are at loss to know what to do. The personal history indicates that the patient has been a slave to coffee and tea for years. Here, too, an explanation to the effect that coffee and related beverages are partially the cause of the illness and inimical to a favorable progress toward health, usually results in satisfactory cooperation, and the error is eradicated. The same, in essence, may be stated of the various spices, condiments, and other harmful substances of food and drink.

One of the most difficult problems facing the internist is the prohibition of the use of tobacco in persons addicted to the use of the weed for many years. Extra-systole and the various cardiac arrhythmias and even auricular fibrillation are more commonly seen in tobacco users of this class of individuals than in others. Unless the habit is stopped at once, all other efforts to assist our subject will prove fruitless. It is my custom to have the patient promise faithfully at the first visit never to touch tobacco again. I do not permit them to say "I'll try" or "I'll do my best," much less do I permit a gradual weaning away

from the weed. Anything less than "I shall" implies effort with a minimum of determination and is a poor psychological procedure; "I shall" is usually successful; the patient stops using tobacco, and that is all there is to it. I frequently explain that a part of the tobacco habit consists in giving the muscles of the mouth something to do; the taking of chocolate coated nuts, chocolate peppermints, or crackers, when the craving for tobacco arises, will accomplish the same purpose, and these substances being nutritious, will at the same time improve weight and increase strength.

Though a goodly percentage of predisposed individuals possess normal weight and a few are to a degree obese, most are undernourished. These subjects require an avoirdupois to correspond at least to their height and age. Indeed, a ten per cent increase in weight above the person's standard is highly desirable. The surplus serves as a safety point representing an amount of reserve to be relied upon in case of emergency stress and strain. These subjects are commonly poor eaters, though the appetite may be good or excessive. Many have sharp hunger several times a day, but it is quickly satisfied, unsustained and capricious. Thus in response to hunger, the intake of food is equivalent to one-half the customary meal, and this, repeated throughout the three meals per day, corresponds to a smaller daily intake than that of the average individual. Even an occasional "bite" between meals does not yield the number of caloric units required by a person of similar age and stature. The patient has accustomed the stomach to hold comfortably just so much and no more at a sitting, as a result of which the taking of a normal quantity of food causes discomfort. Correction should aim at persistent endeavor to accustom the organ to take at least a normal quantity of nourishment daily, irrespective of discomfort and other apparently undesirable consequences. In the course of several weeks of forced feeding, the subject finds himself eating plentifully, the weight reaches normal and soon above normal, and the ten per cent excess, our goal, is attained. A proper stomach capacity is now permanently fixed; the weight is indicative of a more normal resistence to physical and mental emergencies.

The question of occupation is frequently a serious one. Aside from possible physical deterioration resulting from the

pursuit of certain occupations associated with undue physical exertion, poisoning by lead, phosphorus, arsenic, mercury, and various noxious gases and impurities, there are occupations in which mental strain is a vital factor. Telephone operating with its nerve-racking incidents, school teaching, with its well known potentialities for restless working hours and quite as restless hours off duty as a consequence, social work among the poor and suffering, with its depression—these pursuits, though in the abstract the choice of the persons whose lives are devoted to the work, still carry with them very deteriorating influences upon body and mind. And if we take into account the numerous instances in which the occupation of an individual, such as manual labor, salesmanship, stenography, housekeeping,* and divers other pursuits are forced upon the person in question, and far from being a pleasure, are a perpetual drudge and torture to life, especially in the cases in which there is too little leisure and too much work, we can readily see how important is an investigation of the influence of the daily duties of the person under our study. We must not ignore the occasional unfortunate case of the man or woman of leisure who has become overly introspective for lack of something else to do. Lastly, there are a few occupations which, though not a drudge to the person in question, are associated with the *possibility* of acute mental or emotional strain, which possibility may serve as a sword of Damocles. Among these may be mentioned employment on the topmost floor of a tall building, with its possibilities of fire or elevator accidents, employment in locations where explosions are possible, as in or near chemical laboratories and munitions plants, and others of like nature. Our task must entail an attempt at elimination, or at least reduction of occupational faults which interfere with the maintenance of an equilibrium between internal bodily conditions and external circumstances.

An ominous subjective symptom in this class of individuals is persistently unrefreshing sleep with or without disturbing dreams. A person of this sort frequently arises in the morning feeling not refreshed, rested, and ready for the day's work, but

*The housewife often presents a problem entirely her own. Especially is this true in the presence of children and the absence of a servant. The manifold routine duties of kitchen work, looking after the children, house cleaning and the like, with almost no outdoor air and social existence, deteriorate physical and mental health and serve as a potent predisposing factor in the production of Graves' disease.

fatigued, weary, and anxious to remain in bed, irrespective of the hour and caring little for breakfast. Such a status, occurring daily and prolonged for months or years, is a strong predisposing factor in the development of Graves' disease, and should be overcome by sane, persistent remedial measures calculated to induce healthful, refreshing sleep for at least eight out of twenty-four hours. It may be discovered that nine and even ten hours of sound sleep daily are required in order to secure the necessary physical and mental well-being. In this respect every person is a law unto himself, and the peculiarities of each subject must be investigated and evaluated without any hard and fast adherence to conventional standards. In general, the patient with a known predisposition to Graves' disease should be encouraged to devote an *extra* hour or two each night to sleep or relaxation, for the purpose of reinforcing the autonomic and endocrine stability against possible disturbing influences through the waking hours.

The strenuous life of the times—the mad rush to earn the dollar and the equally mad tear to spend it—coupled with the tendency in some quarters to illicit affections and its implications—all these and allied factors cannot be ignored in the consideration of causal relationship and the prophylaxis of Graves' disease.

Were a careful sexual history obtained as a routine procedure, very valuable information would be elicited, facts which are otherwise missed to the detriment of the patient. Often we find that the sexual perturbation of puberty and adolescence, and indeed the thyroid hyperplasia are continued indefinitely on into adult life. In both sexes, the sexual and emotional restlessness should be tempered by appropriate social, emotional, and aesthetic influences. The status of being affianced, marriage, and pregnancy, in addition to the general sexual thoughts of the individual, are subjects which cannot be overestimated in this respect; it is here, perhaps, more than elsewhere in the consideration of the prophylaxis of Graves' disease in the adult female that common sense and vigilance should be exercised.

Faulty mental habits are almost the rule in these subjects. Aside from those already implied, temperament or disposition must be so influenced as to approximate the ideally consistent as closely as possible. Many possess an undue hypersensitiveness; they are "thin skinned" and often pessimistic. Though high

colored in attitude when things are to their liking, trivial difficulties and obstacles may turn tables so completely that moodiness, gloom, tears, and even hysteria prevail. To change this vascillating mental make-up into one of dependable stability, permeated by a healthy quality and quantity of optimism, though a difficult task, can at least in part be accomplished through the subtle influence of tactful friends or relatives, or under the guidance of a capable mentor. How to increase the threshold of emotional reaction is the vital problem. The substitution for a state of emotional alertness or *qui vive* by an attitude of *sang froid;* in other words, the assumption of the so-called "phlegmatic" temperament by one to whom every mole hill is a mountain, is the "consummation devoutly to be wish'd."

Though the prevention or reduction of the predisposing influences of Graves' disease may appear an abstruse affair, vague in its deductions and in many instances difficult of conception, much can be done by an inculcation into the individual of principles which, in course of time, would diminish discord and increase equilibrium between inherent peculiarities and susceptibilities on the one hand and controllable habits and environments on the other. The adherence to the broad principles of the *simple life** and the discovery and fortification of weak links or vulnerable points in the subject's make-up, with an eye to individualization, will finally bring about the desired equilibrium in sufficient degree to be highly gratifying to all concerned. Having attempted the achievement of this objective, the next consideration is the avoidance, as far as is in our power, of the known exciting factors.

PREVENTION OF EXCITING FACTORS

If in most persons with a susceptibility to Graves' disease we can prevent the occurrence of an exciting factor, the chances are highly in favor, not only of the enjoyment of relatively good health, but also of unusual longevity. In the absence of an attack of the disease, these persons, for some unaccountable reason, are known to exceed the span of three score and ten, and occasionally approach and even reach the century point.

The exciting factors are far more tangible and traced with

*The best place for a subject of this type to reside is away from the seashore; preferably in the country and at moderate altitude, if possible; —a place where the simple life most likely characterizes existence.

less difficulty than the predisposing causes. Given a subject of the type above described, place him in an automobile going at the rate of 40 miles an hour, and rush the machine across railroad tracks just in time to avert a collision with an approaching train, and the mechanism of Graves' disease is begun. There need not be an accident. Psychic trauma, with or without physical injury, is the most usual history obtainable as the starting point of Graves' disease. Following an earthquake, or a fire in a large factory in which many are employed, a massacre, the wreck of a liner in midocean, experience on the firing line in battle, or in other situations of imminent danger to life, forty-nine out of fifty persons soon recover physical and mental poise and are themselves again. One of them, however, because of the singular susceptibility, may evince no psychic and endocrine recoil or adjustment to the previous neuro-endocrine balance. The trembling, the staring eyes, the cold, clammy skin, the heart hurry, and other features expressing fright, remain, become chronic or "frozen," and we are confronted with a case of Graves' disease. The torch of an exciting cause in the form of the acute emotional strain or psychic trauma, applied to the inflammable subject, means a beginning of the syndrome of the disease. Earthquakes, lightning storms, tidal waves, and other natural phenomena which engender many cases of Graves' disease, are beyond human effort to control. War conditions, conflagrations, explosions, elevator accidents, shipwrecks, massacres, automobile and train accidents, and other conceivable situations associated with danger to life and limb are man-made and therefore at least partially avoidable. Unfortunately, these conditions are not in the power of doctors or psychologists materially to control, and therefore not substantially amenable to their prophylactic efforts. It is reasonable to assume, however, that even if exciting causes cannot be averted, if we succeed in reducing in a given subject the degree of susceptibility to the affection, the onset of Graves' disease may be prevented.

Certain circumstances characterized by less acute but more sustained emotional strain and which ordinarily serve as predisposing factors, are likewise exciting causes. Especially is this true if the predisposing errors in question become intensified, and if the susceptibility of the individual is unduly great. It is from this class of subjects, the small minority, that we fail to

elicit a history of psychic trauma or acute emotional strain as the starting point of the syndrome. Extreme illness or the death of a loved one, emotion such as hate, anger, jealousy, and the prolonged strain of such occupations as school teaching, telephone operating, and the like, unrequited love and sexual maladjustments may serve both as predisposing and exciting causes. With regard to the latter, it must be emphasized that sexual neurasthenia, priapism, and impotence in men, and in women prolonged engagements, sexual incompatibility, vaginismus, sterility, multiple pregnancies, and allied conditions, are potent exciting causes and largely amenable to prophylaxis, depending upon the tact and skill of the medical attendant.

Focal infections, though regarded by many as the most important of exciting causes of Graves' disease, are in my experience more often coincidental than causal in the majority of instances. Though I firmly believe that focal infections should receive proper attention, whether in tonsils, teeth, nasal sinuses, gastro-intestinal or genitourinary tract, the percentage of patients actually cured by tonsillectomy, removal of teeth, gall bladder, appendix, colon, and other parts of the body found to be at fault, is remarkably small. That a causal relationship has been assigned to a mere coincidence is obviously the case in many patients. It must be insisted upon, however, that irrespective of their etiological importance, focal infections require prompt attention.

Frequently tuberculosis and syphilis, and occasionally acute rheumatic fever, are provocative of the syndrome of Graves' disease, and require expert management. The same may be said of autointoxication, whether it be renal, biliary, or intestinal.

Neoplasms, especially fibroids of the uterus and adnexia, are at times exciting factors of Graves' disease. I have observed a few instances of startling amelioration of the syndrome following the removal of a uterine fibroid. But in a discussion of the relationship of a nonhyperplastic thyroid growth, a note of caution must be sounded, lest erroneous etiological theories of Graves' syndrome be entertained. A thyroid adenoma, in course of time, may give rise to hyperthyroidism, and thus we are confronted with the so-called toxic adenoma. This is not synonymous with Graves' disease, and the removal of the adenoma cures the patient. On the other hand, Graves' disease is not due to hyper-

thyroidism, but to a generalized dysfunction of the autonomic nervous system and of the entire endocrine chain; hence thyroidectomy is disappointing in the therapeutics of the affection.

The prophylaxis of Graves' disease must also include a consideration of the prevention of relapse after recovery from an actual attack. In all patients in whom complete recovery has been firmly established and maintained for a year or longer, we may safely assume that the predisposition to the disease has at least been materially minimized, if not altogether eliminated. This is especially true of patients in whom thyroidectomy was not depended upon, but who were fortunate enough to have been under the care of an experienced internist, with resulting approach to the normal or arbitrary standard of bodily and psychic health and the usual resistance to Graves' disease. Such a person, having recovered from this dread affection, has been habituated during treatment to obedience to the required principles of hygienic, dietetic, and mental daily life. Taught how to eat, how to work, how to sleep, and even how to think, this individual is living practically an "anti-Graves' disease" existence, and has become more useful than ever to self and society.

CONCLUSIONS

1. Prophylaxis of Graves' disease by individual and organized effort is timely and important. The devotion of more time and energy by internists and general practitioners to the study of the diagnosis, prophylaxis and treatment of this affection would not only reduce the number of sufferers, but would in course of time place the therapeusis of Graves' disease on a strictly nonsurgical basis.

2. Ideal prophylaxis of Graves' disease should begin in infancy and extend well into adult life, the object being an attempt at perfection in hygienic, dietetic and mental discipline.

3. During childhood, such additional influences as school and home life, companions, recreation, and other factors capable of molding the physical and mental self must be taken into account.

4. During the restlessness of puberty and adolescence, the emotionalism, instability of reasoning processes, and the physiological thyro-gonadal hyperplasia, all make for an accentuation of neuro-endocrine instability, and should receive most thoughtful, scrupulous guidance.

5. In general, an individual standard of conduct to self and the outside world must be formulated for these individuals. It is a two-fold task—each contributing equally to the achievement of the goal, viz.: (a) the adjustment or adaptation of the circumstances of life to the singular peculiarities of the individual, and (b) the modification and adaptation of the peculiarities of the individual to the circumstances of life.

6. Predisposition to Graves' disease is not always markedly amenable to prophylaxis, nor are exciting causes of the disease always avoidable. In the absence of the ideal (the *eradication* of predisposing and exciting causes), if we can *reduce* susceptibility on the one hand, or *modify* the *chances* of the occurrence of exciting factors on the other, the prophylaxis of Graves' disease will have earned an important place in preventative medicine.

7. The question involved is not that of a "lump on the neck." We must firmly understand that a subject of Graves' disease is no more a victim of goiter than is a sufferer with typhoid fever one of splenomegaly. The elimination of this disease from the classification of goiter is the first real step toward a better understanding of the etiology, prophylaxis and treatment of this, the most interesting affection in the domain of medicine.

HYPERTHYROIDISM: A NEW CLINICAL SIGN

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It has no doubt occurred in the practice of many clinicians that in a short period of time several cases of the same type have appeared for examination. Krehl called this the "Duplicitate die Felle."

In the course of the physical examination of patients, a group presented themselves with a certain objective finding, the exact clinical significance of which was not appreciated until it recurred again and again, and finally registered the impression that its occurrence was something more than an accidental symptom of no especial value.

Just behind and below the sterno-clavicular junction, about 1 to 2 cm. either to the right or left, is the anatomical position of the inferior thyroid artery. Over this area a bruit is heard which is unlike the murmur over the gland when it is visually or palpably enlarged. In fact it may be present when both of these factors are absent. This sound is *hissing* or siren-like in character as differentiated from the *whirring* or water-wheel churning sound heard over the gland itself. The hissing character of the sound over the artery is the point I would emphasize as new and distinctive of hyperthyroidism, or of potential hyperthyroidism. The sound is heard more frequently on the right than on the left side, but in marked cases when there is considerable evidence of thyreotoxicosis it is present on both sides. It is not transmitted to any of the other blood vessels of the neck or superficial vessels of the trunk or extremities, and I have never heard it over the superior thyroid vessels. It is increased by deep inspiration, and is not lost during expiration. It is systolic in time and is lost during the rest period in the cardiac cycle. Accompanying the hissing bruit, but with no definite degree of constancy, is a palpable thrill in the cubital artery.

In all, it was present in 12 cases, 2 men and 10 women. Without going into the detailed history of these cases, which is

immaterial for our purpose of discussion, the exciting causes which led to the hyperfunction of the thyroid may be classified as follows: Brain work or mental strain, puberty, tuberculosis, pregnancy, excessive intercourse and toxic conditions, *i. e.*, septic tonsils.

This observation extends over a period of about one year, during which time as a matter of routine all patients were examined to determine whether or not this sign occurred in conditions other than hyperthyroidism, and included a number of normals. Especial care was exercised in the examination of high blood pressure cases, particularly those of 200 or over, and one case of over 300 in which I was unable to measure the pressure because of lack of markings on the instrument. No evidence of the bruit was found in any of them. I was unable to produce the hissing bruit by pressure or manipulation of the bell of the stethescope on any of the arteries, in any cases other than those in which the subjective symptoms checked with the objective signs and justified the diagnosis of hyperthyroidism.

The diagnosis of hyperthyroidism was checked by basal metabolic determinations and the estimation of the sugar tolerance. In some cases the rate was normal, in others it was increased. The sugar curve showed an analogous variation from normal to retention with the presence of sugar in the urine. These findings are consistent, however, with available clinical data, as there are cases of toxic goiter reported in the literature with a normal basal metabolic rate.

Another striking characteristic of the bruit is its evanescence. It is not constant, but is apparently dependent upon the heart action for its production. In those cases in which the heart action is accelerated and there is a precordial thrill, the bruit is present, as is also the cubital thrill. With the general amelioration of the symptoms, due to rest or the administration of iodine, these signs disappear. This clinical fact is not at all at variance with certain experimental work, and with clinical observation carried out on a large series of cases. It would appear, then, that its production is dependent, first, upon an accelerated and increased heart action, and, secondly, upon a consequent increase in the rate of the blood stream. The possibility of a third condition, namely, arterial changes having an influence, will be discussed later.

Plummer (1) has shown that "if a patient, having a colloid goiter with bruit, thrill and palpable thyroid arteries, is given 5 to 10 mg. of thyroxin intravenously, or a corresponding dose of desiccated thyroid by mouth, the bruit will diminish in from three to six hours, the thrill and palpability of the arteries will disappear in from twenty-four to thirty-six hours. This reaction takes place in all cases." The bruit referred to in the literature is the one heard over the gland itself, as I find no reference or description of the hissing bruit over the blood vessels in any of the writings on the clinical evidence of hyperthyroidism.

The circulation in hyperthyroidism has always presented an interesting problem to the clinician. While the preponderance of study on thyroid disease has been done by the pathologist on the gland itself, there still remains to be explained certain constitutional manifestations and symptoms which pathologists do not clarify. The clinician is reluctantly forced into the field of theory in order to explain them. It has been said that "in the analysis of most clinical as well as didactic problems, much that is not definitely known must be bridged over by theory." If, then, we build our theoretical bridge and prop it by our clinical experiences, looking to the pathologist for reinforcement, we may be able to build a structure that will stand the weight of further investigation.

The pounding, heaving pulsations of all of the superficial blood vessels in thyroid hyperfunction, coupled with a palpable increase in the thickness of the vessels and a rise of blood pressure, lead to the thought that besides the local effect on the thyroid itself, an increase of circulating thyroxin must exert a constitutional effect upon the arterial system which is more or less lasting.

In the terminal branches of the arterioles where the muscle tissue predominates, there is opportunity for great expansion and strong contraction. Since this mechanism is under the control of the sympathetic system, which is also involved in hyperthyroidism, it is not too much to assume, from a clinical standpoint, at least, that this vasomotor instability produces an increase in the muscle coat of the systemic arterioles, with a concomitant influence on blood pressure. This influence exerted on the heart brings about left-sided hypertrophy, increased blood pressure, albuminuria and other symptoms found in hyperthyroidism,

which are referable to arteriosclerotic changes. Let us see for the moment if this theory finds substantiation in the pathological studies on the gland.

Crile (2) has mentioned the fact that in many cases of goiter the superior and inferior thyroid arteries are considerably increased in size so that a distinct pulsation can be felt throughout the entire gland.

Wilson (3), whose description of the pathology of the vascular changes within the gland in exophthalmic goiter is the most exhaustive I have found in the literature, is of the opinion that the gland is hyperemic, and that this condition is demonstrable both grossly and histologically; further, that this increase in vascularity is not due alone to an increase in the size of a few large arteries and veins, but also to a diffuse general increase in the size of the small arterioles and capillaries.

Kendall (4) states that "the immediate effect of an intravenous injection of thyroxin causes no change in blood pressure, pulse rate, nervous manifestations or other hyperthyroid symptoms; but the long continued presence in the tissues of the body produces the picture of hyperthyroidism, ending in great emaciation and death." It was, therefore, demonstrated that the long continued presence of thyroxin caused death from secondary reactions and not from its direct toxicity.

Sistrunk (5) is of the opinion that while some patients improve under medical treatment, it is unwise to allow it to continue over too long a period of time because they are apt to have marked degenerative changes in their vital organs.

If we assume the toxic origin of the changes in the blood vessels to be true, we may ask ourselves two perinent questions.

1. Is there an analogous condition of the blood vessels found in which similar murmurs are heard?

I recently examined a case of arterio-venous aneurysm, in which I was impressed with the similarity of the murmurs. In this patient the hissing murmur was present in practically all of the blood vessels, not only in the thigh, but also in the femorals, illiac and thyroid vessels; in fact, all of the superficial blood vessels. The case was parallel to the one reported by Osler (6), in which a patient with circoid aneurysm developed multiple aneurysms following typhoid fever.

A case in point was reported by Fernell in the St. Louis

"Courier of Medicine" in 1887. "A man, aged twenty years, had a large pulsating tumor above the clavicle, which had lasted many years and which involved all of the branches of the thyroid axis, except the inferior thyroid. During an attack of measles the temperature rose to 106.5 and the tumor looked red and angry and pulsated very strongly as if about to rupture. Following the attack of measles the tumor began to subside gradually, the thrill disappeared and it shrank to a mass of hard connective tissue which could be rolled about. It has further been shown that no structures retain their powers of growth in greater degree than the arteries. Many physiological conditions demand the retention of this property; for example, the arteries of the uterus at term are four or five times as large as in the unimpregnated state."

These examples of the capability of the arteries to change in caliber and lose certain apparent pathological conditions by a peculiar and innate power of size regulation which is essentially their own, serves in a striking manner to illustrate the point with regard to the presence and absence of the hissing sound as controlled by the improvement of the patient on the one hand, and the toxic origin of the changes on the other.

2. Can the murmur be produced by reaching the physiological limit of thyroid medication in hypothyroidism?

I have seen two such cases, one in a child six years of age and the other in an adult.

Following the administration of desiccated thyroid extract for a period of two months the child grew two inches and gained six pounds. It then developed a tachycardia, was nervous, and on listening over the inferior thyroid, the hissing bruit was heard. The gland was not palpably enlarged. The adult case presented practically the same result, except for the fact that the symptoms of hyperthyroidism were much more pronounced. There was extreme nervousness, insomnia, sweating and distressing tachycardia. This experience demonstrates that with the physiological development of the hyperthyroid state, the hissing murmur develops as a part of the clinical syndrome.

In the back swing of the pendulum from its long upward flight, accelerated by the enthusiasm placed on the value of the increase of the basal metabolic rate as a pathognomonic expression of hyperthyroidism, and the failure of the constancy of the

glucose tolerance test, the clinician again finds himself struggling with the same problems of diagnosis which he met before the laboratory was called upon to aid in the interpretation of clinical problems. The more one sees of negative laboratory findings the greater should be the impression upon the mind of the diagnostician that more thought, time and energy must be given to the upbuilding of objective clinical signs, which are independent of the laboratory and through the development of which the value of thorough physical examinations will be greatly enhanced.

The pathologist should not be expected, even by a careful study of the tissues, to give a true interpretation of the clinical symptoms of a given disease and, vice versa, the clinician should not be looked to for a pathological diagnosis. It is in such misdirected attempts that errors in clinical diagnosis are inevitable. The fitting together, however, of these two elements will hasten the day of the ideal in medicine, and will elevate the art of diagnosis to the pedestal from which it has been so ignominiously removed.

From these studies I have come to the following conclusions:

1. The hissing murmur in the inferior thyroid artery is associated with toxic hyperthyroidism.

2. There are pathological changes found, for the most part in the systemic arteries, due to circulating thyroxin when present for an extended period of time.

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EXOPHTHALMIC GOITER FOLLOWING VARICELLA AND MASTOIDITIS IN A CHILD WITH STATUS THYMOLYMPHATICUS

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Buford (1), who has recently reviewed the incidence of Graves' disease in young children, states: "I have reviewed both American and foreign literature carefully for the last twenty years and find eighteen cases reported in children under twelve years of age. I find only two cases in which operation has been performed. My patient (third to be operated) was six years old, the youngest one that has been reported as operated." Nine cases, including the one reported by Buford, have been reported in children under five years of age. Another case is herewith presented.

REPORT OF CASE

Case No. C. 966; 5-26-1922; C.C., female, age 4 years and 7 months.

Family History: The father is somewhat nervous, has high blood pressure and a rapid pulse; his eyes are moderately prominent, but apparently normal. The mother's eyes are also prominent. The paternal grandmother died of heart trouble; the maternal grandmother died at child birth; the grandfather died of tuberculosis of the kidney; the aunt has throat trouble; the uncle is living and well.

Chief Complaints: Nervousness, exophthalmos of both eyes, frequent urination, loss of weight and rapid pulse are the most prominent symptoms.

Clinical History: The child's birth was normal. She was very sickly during the first six months. She was weaned early. More or less stomach trouble has been manifest since birth. She has always been high strung, very active, and mentally bright and alert. She had more or less trouble with the glands of the neck. She was talking at 12 months; lisping was noticed early. She sat alone at 8 months, crept at nine months, walked at 18 months, and laughed aloud at 4 months. She got her first tooth at 7 months, and had a full set at 2 years. She had influenza and tonsilitis in 1920. The tonsils and adenoids were removed in 1920. She had chicken-pox early in 1922. She complained of mastoiditis, April, 1922.

The present conditions developed following chicken-pox in April, 1922, and continued up to the time she consulted me. An operation for the relief of the mastoid condition had not been deemed advisable by her otologist. The eyes, although normally large, rapidly gained prominence following the attack of chicken-pox. The patient weighed

Age	*Measurements* Weight (Pounds)	Height (Inches)	Chest Cir. (Inches)	Head Cir. (Inches)
Birth	7.75	21.50	14.00	15.75
6 months.....	13.50	26.00	16.50	17.50
12 "	21.00	29.50	17.50	19.00
18 "	25.00	32.50	20.00	20.00
24 "	28.00	34.75	20.50	20.50
36 "	32.00	38.00	21.50	20.50
55 "	36.00	44.50	....	....

40 pounds prior to the onset of mastoiditis, lost 10 pounds during the active stage of her trouble and weighed 36 pounds at the time of examination. Along with the development of eye symptoms there appeared tachycardia, gastrointestinal irritability as evidenced by attacks of vomiting and a tendency to diarrhea, and an overwhelming lassitude in spite of her extreme restlessness and emotional excitability. She complained at times of pains in the back, hips and arms. The pulse ranged from 110 in the early morning to 140 at night. There was frequent desire to urinate; sphincter control was normal. Sleep was not sound nor restful. Vomiting attacks occurred frequently—"on the slightest provocation." These attacks were associated with yellowing of the skin and marked dehydration. There was marked nocturnal diaphoresis at times.

Physical Findings: The patient is 44½ inches in height, 36 pounds in weight and is poorly nourished. Her skin is moist and of fine texture. Her blood pressure is 90/45; pulse, 148 lying down; buccal temperature, 99°F. She has an abundant head of hair, dark, of fine texture, and with moderately low anterior attachment. The

Fig. 1. Photographs showing the degree of exophthalmos and the small degree of enlargement of the neck due to hyperplasia of the thyroid.

eyebrows and lashes are well formed; hair is absent on the remainder of the body. The eyes markedly protrude. The sclera show above the cornea when the patient looks straight ahead; there is marked widening of the palpebral fissures (Dalrymple and Stellwag's sign), and weakness of convergence without diplopia (Möbius' sign); involuntary blinking is infrequent (v. Stellwag's sign); other eye symptoms are hippus, large pupils, dryness of the eyes, inability of the upper eyelids to follow the descent of the eyeball (v. Graefe's sign), fullness of both upper and lower lids, pale conjunctivae, no tremor of the lids nor nystagmus of the orbs. The lids can be forcibly closed over the cornea; pressure on the orbit slightly accentuates the pulse; pupillary reflexes to light and distance are lively.

The ears are large and set at a wide angle to the head. There is tenderness over the mastoids. The cervical and inguinal glands are

palpable; the tonsillar fossae are empty; because of adenoids breathing is through the mouth. The teeth are in fair condition, small and pearly white. The palatal arch is high; the speech is lisping; the voice is high pitched and rather harsh; there is a tendency to drool; there is a dry, unproductive cough.

The neck is full, showing anterior and lateral enlargement of moderate degree; there are marked pulsations; the goiterous mass is soft.

The heart rate is rapid—145 to 148 when lying down; there is no arrythmia; a musical systolic murmur is heard best at the base of the heart, transmitted to the upper left chest and neck; a distinct thrill is discernible over the left infraclavicular region; the area of cardiac dullness is increased in all diameters. Mediastinal dullness is marked, wider than the sternum.

Breathing is shallow and rapid, 25 to 40 per minute; sighing is frequent; respiration is of the abdominal type; breath sounds are rough; there are no rales. The patient is pigeon breasted and has a prominent abdomen. She would not permit palpation of the epigastric region.

Reflexes are very active, but otherwise normal. The rectum, genitals, spine and joints are negative. Muscular development is poor; fat deposits, light. Coordinated movements are executed gracefully. There is slight gross tremor of the extended hands, but no Rombergism. She is continually fidgeting and talking, is of a friendly, good-natured disposition, and is keenly interested in her surroundings. A mental test made by Dr. Stevenson Smith, who referred the case to me, showed the physical and mental ages to be equal, *i. e.*, normal mental development for her age.

Laboratory Findings: The urine has a specific gravity of 1022, is alkaline and contains no sugar, albumin nor casts; phosphates are abundant. The blood is made up of: hemaglobin, 80 per cent; erythrocytes, 3,600,000; and leucocytes, 6,800; the differential count shows neutrophiles 36; small mononeuclear 59; large 5. Dr. K. J. Holtz reports the results of a radiographic examination as follows: "Heart shadow enlarged; unable to differentiate aortic shadow from others in the mediastinum. Mediastinal shadow approximately 3 inches wide, regular in outline, continues from the heart shadow upward into the neck. Inflammatory areas in the region of the hili, particularly on right side; probably glandular. Epiphyses of wrist and hand open."

DIAGNOSIS

The case was diagnosed as exophthalmic goiter and status thymolymphaticus.

TREATMENT AND PROGRESS

Because of the size of the thymus gland and the known risk of operative procedures in patients with status lymphaticus it was deemed best first to attempt reduction of the gland by radiation and later to ligate the thyroid arteries or remove a part of the thyroid gland, depending upon her progress.

On May 31, 1922, the pulse was 144; blood pressure, 88/35 to 50; temperature, 98.8°F. On June 2, the patient received 84 milleampere minutes' radiation over the thymus area (distance 16 inches, gap 8¼ inches, 4 mm. aluminum filter). During the

afternoon the child ate ice cream. She vomited several times that night. Nausea and vomiting continued until June 5. During that period the pulse varied between 124 and 148. The temperature remained normal. June 30, the patient spent a week in bed following her arrival home, suffering from a "bilious attack." During that attack her skin did not turn yellow as upon previous occasions of a similar nature. The urine at this time, as upon June 5, showed numerous granular casts, considerable albumin and a great amount of solid material including urates. Her sleep had been greatly disturbed since radiation. The appetite was variable; the stomach, extremely irritable; there was diarrhea with mucus in the stools; and short sighing respiration.

July 1, a radiogram showed marked decrease in the diameter of the substernal shadow. Hili shadows were prominent with considerable lateral radiation. The patient received a second x-ray treatment over the thyroid area of the same strength as the first. Within a few hours following the treatment nausea and vomiting set in and continued until July 5. On July 3, the evening temperature was 100.5°F.; pulse, 150; respiration, 40. On July 4, the temperature was 99°F.; pulse, 150; respiration, 40. The urine showed but a few casts and pus cells, considerable albumin, and much solid material. July 8, the pulse was 104; there was no elevation of temperature; the urine was greatly improved. After this the patient returned home and passed from observation.

DISCUSSION

It appears that my patient showed signs of lymphatism soon after birth. This condition was evidenced by the enlargement of follicles at the base of the tongue and pharyngeal lymphatic growths in the nose. The enlargement of the tonsils led to their early removal and, as usual for this type of case, "she has never been right since."*

It is likely that the attack of influenza during the same year as the removal of the tonsils and adenoids aggravated her condition; however, it was not until after an attack of chicken-pox that the thyroid disturbance became manifest. Two months following the onset of chicken-pox she contracted mastoiditis. This infection greatly and rapidly accentuated the thyroid symptoms.

*Similar results followed removal of the tonsils in a young girl seen by me in St. Louis, in whom a large thymus gland was found and successfully treated by the use of the x-ray.

The series of infections, it seems, might be considered as a causative agent in the production of the hyperplastic goiter. This assumption is in accord with the findings of McCarrison *et al.* To quote Janney (2), page 800:

"The hyperplasia of thyrotoxicosis is best explained, just as in other thyroid hypertrophies, as an attempt at compensatory regeneration to make up for cellular exhaustion and injury due to toxic or other causes. We have thus an acceptable explanation for the thyroid hyperplasia of Graves' disease arising from local or focal infections, intestinal toxemia and bacterial infections—hyperplasias not susceptible of reasonable explanation by the hyperthyroid theory."

Adler (3), in 1917, contended that diseases of the thymus are able to produce Graves' disease with or without disease of the thyroid. He concludes that his experiments prove that Graves' disease never is due to an abnormal function of the thyroid, but that the goiter is caused by Graves' disease. In Graves' disease, according to Klose (4), the thymus is next to the thyroid in importance in that it undergoes morphological changes—"epithelization." The two glands can cause a general hyperplasia of the lymphoid system. Simpson (5) calls attention to the frequency with which exophthalmic goiter is associated with enlargement of the thymus, and advises that x-ray therapy precede operative measures on the thyroid. According to Janney (2), page 806:

"A diffuse adenohyperplasia is regularly found in Graves' disease (Kocher, F. v. Müller). This may include the tonsils, spleen, and intestinal follicles. The lymphoid cell infiltration of the thyroid itself is best considered an expression of the same general process. It is probable that the thymic enlargement, in spite of efforts to bring out a more specific relationship, is but an instance of the general *status thymolymphaticus* present (Capelle; Eddy). The lymphocytosis and mononucleosis present in both hypothyroidism and exophthalmic goiter are probably due to this *status lymphaticus.*"

Melchoir (6) points to the fact that the thymus is large in from 75 to 85 per cent of patients suffering from Graves' disease. Nordmann (7) believes it necessary in every operation for Graves' disease to look for the thymus. In patients with symptoms of status lymphaticus or hypoplasia of the sex organs the

thymus should be removed before attempting operative measures on the thyroid. Haberer (8) also is of the opinion that thymus destruction should constitute a part of the treatment of patients suffering from an enlarged thymus and Graves' disease.

From a review of the literature it is concluded that the proper management of patients suffering from Graves' disease and status thymicus is destruction of the thymus gland by the use of radiation and the surgical removal of part of the thyroid gland. Such a line of treatment was planned for the present case; however, because of withdrawal of the patient, this could not be carried out.*

Thymic destruction because of radiation was evidenced in my patient by the marked decrease in the size of the organ as shown radiographically and by the appearance of a great amount of solids in the urine. Further, it appears probable that the rapid destruction of the gland and the consequent demand made upon the excretory organs was the causative agent in the production of the transient nephritis following x-ray therapy. This assumption is more convincing when it is recalled that the urine was negative as to albumin and casts before such treatments, although the patient was convalescing from an attack of mastoiditis.

The blood picture in the present case appears to be that of lymphatism; however, as is well known, a lymphocytosis is characteristic of exophthalmic goiter [see quotations from Janney (2)]. The leucopenia perhaps gives at least an associative explanation for the frequency of, and low resistance to, infections. It therefore appears that the reduction in the number of polymorphonuclear cells, even at a time of mastoiditis (a condition usually not associated with leucopenia), was one of the predisposing factors to the repeated infections which finally resulted in the production of a toxic goiter.

CONCLUSION

Consideration of the present case suggests a definite relationship between infectious processes and the development of a

*The patient underwent an operation for partial thyroidectomy by her local physician soon after her last x-ray treatment. The pulse, according to her mother, ranged between 94 and 140 after the operation. The weight increased to 52.5 pounds. Her rest, appetite and general condition became greatly improved. There was cessation of vomiting and increased bowel activity. She lost weight during a recent attack of grippe.

On April 4, 1923, an examination showed the pulse to be 102, standing. Her weight was 47.5 pounds and her height 47.25 inches—a gain of 2.75 inches in 10 months. The exophthalmos was somewhat reduced. There was but a slight coarse tremor of the extended hands.

toxic goiter. Further, it appears that the state of lymphatism was either a predisposing cause of infection, or it permitted a more toxic condition because of a lowering of the efficiency of the mechanisms of defense. If these two suppositions are justifiable, then it follows that the toxic goiter (Graves' disease) is the result indirectly of lymphatism and directly of infection.

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Book Reviews

SEXUALREFORM UND SEXUALWISSENSCHAFT. Edited by Arthur Weil, Stuttgart, 1922. Julius Püttmann. 288 p. 8°.

This book is a collection of the papers and addresses presented at the first international congress for sexual reform and the fundamentals of sexual science, held in Berlin. After a section devoted to introductory addresses some 80 pages are given to the second title, "The significance of the internal secretions for human sexuality." Under this heading nine articles are presented.

1. Die innere Sekretion der Geschlechtsdrüsen und ihre Bedeutung für die Sexualität des Menschen. pp. 8-14. Alexander Lipschütz.

This is a general article treating of the evidence and theories of interstitial cell function.

2. Die Bedeutung der endocrinen Systems für die Sexualität. pp. 14-27. Artur Biedl.

This is another general article valuable as a concise statement of present-day views in endocrinology by an old master of the subject. Among the topics considered are the morphological differences in the several endocrine glands in the two sexes, changes in each following castration, effects following extirpation of various single glands, and hermaphroditism.

3. Körperproportionen und Intersexualität als Ausdrucksformen der inneren Sekretion. pp. 27-31. Artur Weil.

The author has found that the index of "upper length" to "lower length" (measured from vertex to end of vertebral column, and from this latter point to the floor, respectively) shows a distinct difference in the normal male from the female. The same is true for the index of shoulder breadth to hip breadth. In 200 homosexual males the average for each of these indices was distinctly different from that of the heterosexual male and approached that of the female.

4. Die klinische Wirkungen der Vasoligatur (Steinach). pp. 31-48. Peter Schmidt.

A report of 20 human subjects operated upon since 1920. The author is fully convinced of the value of the operation. After a consideration of the experimental work which has been done on animals, several detailed case histories are given. Among the physical results obtained are growth of hair and restoration of pigment, increase in muscular strength, changes in

blood pressure, including increased genital vascularization, bettered vision and return of sexual potency. The author also believes that certain definite psychical results are obtained.

5. Erfarhungen mit der Steinachschen Operation bei der Behandlung der Impotenz. pp. 48-49. E. Littaur.

Sixteen cases are reported, and the operation briefly described. The author is convinced that the operation is of value in selected cases.

6. Zum gegenwärtigen Stand der Hoden überpflanzung. pp. 49-50. H. Stabel.

That successful transplantation of a testis, following castration performed after puberty, causes a return of libido and potence, Stabel considers an established fact. On hermaphroditism and homosexuality, after these have become established, there is no result. The author considers that reliable evidence concerning rejuvenescence through testicle transplantation has not been obtained. However, the maintenance of libido and potence as well as the secondary sex characters by autotransplantation he considers amply proved.

7. Tuberculosegift und Sexualinkrete. pp. 50-56. R. Gassul.

Observations on 44 tubercular subjects, 29 female and 15 male, ranging in age from 18 to past 40, showed that there was a marked increase in libido in both sexes. The author believes that the heightened libido observed in these cases is, like normal libido, endocrine in nature, and is accounted for by an increased activity of the sexual endocrine glands, induced by the tuberculosis toxin.

8. Die Bedeutung der Steinachschen Forschungen für die Frage der Homosexualität. pp. 56-61. H. C. Rogge.

After a somewhat theoretical discussion of homosexuality the author attempts to explain the condition by assuming that a bisexual gonad is present, having antagonism between the two components, with now predominance of one, now of the other.

The remainder of the book is devoted to a consideration of the moral, social, political and legal aspects of various sex problems.—W. J. A.

Diets and Articles of Food Suitable for Diabetic Patients. R. T. Williamson. Manchester, 1919. Sherratt & Hughes. 35 p.

A very handy little book, giving a very large number of kitchen recipes for diabetic patients. I always tell my patients to buy it and I believe that any doctor treating many cases of diabetes would find it desirable for similar use.—J. K.

PROBLEMAS ACTUALES DE LA DOCTRINA DE LAS SECRETIONES INTERNES. G. Marañón, Madrid, 1922. Ed., Ruiz Hermanos.

Marañón offers a critical revision of an attempt to formulate the present status of endocrinology. He points out the futility of attempting by exaggerated enthusiasm to gloss over the defects of our knowledge in this or any other field. He deplores as puerile and pedantic the credulous acceptance of everything in print as valid data. Until a given question can be answered with a definite yes or no it is still a proper subject for investigation. An unfortunately large proportion of the assumed facts of endocrinology are merely more or less plausible hypotheses; nevertheless our knowledge of the humoral factors has now reached such volume as to justify Gley's claim that endocrinology has revolutionized biology. Endocrinology still presents, however, many unsolved physiological problems relating to metabolism, growth and sexual evolution. Numerous clinical endocrinopathies present themselves insistently for elucidation. Among the positive accomplishments of endocrinology are demonstrations of the value of at least six therapeutic substances. Endocrinology has now entered into a classical period in which extreme attitudes, either favoring or opposing, are futile. It demands the same consideration as other fields of biology. Indeed, the problems that it offers are attractive beyond the average.—W. H.

SIGNS OF SANITY. Stewart Paton, Princeton University. Charles Scribner's Sons, N. Y., 1922. 241 p., 4 pl.

This semi-popular presentation of the essentials going into the make-up of a sound mind and body, together with an exposition of the principles of mental hygiene, has much to commend it not only for the general reader but also for the physician. The interrelations between mental activities and the functions of the glands of internal secretion are touched upon in many places, particularly with respect to the role of the endocrine glands in conditioning the degree of response to stimulation.
—F. S. H.

GLANDS IN HEALTH AND DISEASE. Benjamin Harrow, N. Y., 1922. E. P. Dutton & Company. 212 p.

The author attempts to set forth in terms comprehensible to the intelligent lay public the actual accomplishments of endocrinology in contrast, as he expresses it, with "the half-baked knowledge, worse than no knowledge at all," that the layman often gets. While the book reveals a lack of expert familiarity with the subject of endocrinology, the attempt is on the whole successful.

In the hope that a second edition may soon be required, a few suggestions of changes may be offered. That "every ductless gland" manufactures a "specific substance" (p. 6) is not proved and is probably not true. On page 26 is an ambiguous statement that seems to imply that 2.5 grams is an ounce. The treatment of hypophysectomy (p. 49 et seq.) by no means reflects the actual status of the subject. That complete removal of the hypophysis is necessarily a fatal operations is denied by excellent authorities. Likewise, the relation of hypophysectomy to infantilism is by no means settled. "Progeria" is misspelled on p. 51. Pituitrin is said to have established itself as a "useful diuretic," whereas its therapeutic usefulness appears only in its antidiuretic influence. "Histidine" (p. 56) is misused for histamine. "We know that even under normal conditions the blood always contains a small quantity of adrenaline" (p. 85); this is a bit of knowledge that—if true—should be more widely shared.

It is a matter for regret that in the appended list of references some of the most prolific sources of "half-baked knowledge" of which the author complains are included, as supposedly authoritative.

The foregoing are mostly minor defects and the book is recommended as probably the sanest and most reliable popular exposition of endocrinology in the English language.—R. G. H.

HORMONE THERAPY BY SERA, VACCINES AND DRUGS. D. Montgomerie Paton, London, 1922. Baillière, Tindall and Cox. 164 p.

Contrary to the implication of the title, the book contains little of direct interest to endocrinologists, as such. The author, in the course of the development of some highly original conceptions of the actions of sera and drugs, assumes that the endocrine organs play an important role in tissue resistance. Little evidence of this assumption, however, is offered.—R. G. H.

ENDOCRINE THERAPEUTICS. Thomas Bodley Scott, Philadelphia, 1922. P. Blakiston's Son & Co. 116 p.

This little book is an attempt to present some phases of organotherapy to the general practitioner in an easy, readable way. With the exception of a few personal observations, cited without details, the book is made up largely of theoretical exposition of data taken at third hand from Bainbridge's Elementary Physiology, Sajous' well known work and Berman's recent book.—R. G. H.

THE SEX COMPLEX. W. Blair Bell, London, 1920. Bailliere, Tindall & Cox, 2 ed. 251 p.

The issue of a second edition of this book within four years indicates that, though treating a rather special subject, it has been highly appreciated. The style of the book is very readable, though oversimplified and more or less superficial and incomplete. It deals with secondary and primary sex characteristics and with the interrelations of the different endocrine organs. The last hundred pages are devoted to the pathological and psychical disorders of the incretory organs as related to sexual characteristics.—J. K.

Abstract Department

(ADRENAL)—Hirsutism in a boy of 12. Basal metabolism study (Hirsutisme chez un garçon de douze ans. Étude du metabolisme basal). Apert (E.), Stevenin & Broca (R.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1750-1753.

Typical case of hirsutism, the patient having the basal metabolism of an adult man.—F. S. H.

Paroxysmal severe adynamia in amyloidosis of the ADRENAL cortex (Paroxysmale schwerste Adymanie bei Amyloidose der Nebennerenrinde). Bauer (J.), Klin. Wchnschr. (Berl.), 1922, **1**, 1595-1597.

A man of 66 years complained of oppressed respiration after the least physical exercise. Every day he had 2 to 3 sudden attacks, even being unable to raise his head at times. He died during one of these attacks.—J. K.

Growth of the cortical and medullary substance of the ADRENAL gland and their volumetric relation. Histological-biometric research on Cavia cobaya (Accressimento delle sostanze corticale e midollare della glandola surrenale e loro rapporti volumetrici. Ricerche istologiche-biometriche in Cavia cobaya). Castaldi (L.), Arch. di fisiol. (Florence), 1922, **20**, 33-127.

From measurements of 34 male, and 37 female guinea pigs, and numerous fetuses, and a comparison of these observations with previous results, the author concludes as follows: The inter-renal body is visible in the 7 mm. embryo as an outgrowth of the coelomic epithelium. The immigration of the medullary element has not begun in the 18 mm. fetus, but in that of 32 mm. it is distributed through the inter-renal body, occupying about one-fourth of the whole volume, but not yet giving the chromaphil reaction. Subsequently, while the medulla is drawing together to the centre, it diminishes relatively, and at birth is about one-fifth the size of the cortex. In only two cases was the medulla found much dispersed at birth. The actual weight and volume of the male adrenal is greater than that of the female of like age in both prenatal and post-natal life. The volume, relative to body weight, is greater in the female, even in utero. The left gland is usually larger than the right. The adrenal grows continuously, and increases relatively to body weight. The cortex shows parallel growth, more regularly

in the male; that of the female shows a sudden increase in the second month (puberty). The medulla, compared with total body-weight, shows relatively little increase, with marked oscillation, and diminution during periods of greatest cortex growth, and in old age. In advanced age there is marked absolute and relative cortex increase. The medulla has greater specific gravity than the cortex. It averages one-ninth the volume of the cortex. The ratio is a function of age and diminishes from birth. In the gravid female the cortex hypertrophies; during lactation it returns to normal. In only one animal, a female, was a cortical body visible macroscopically. All the data fall into line with physiological, pathological and clinical data emphasizing the importance of the adrenal, and especially of the cortex, in connection with body-growth. The original paper must be consulted for actual figures.—A. T. C.

Observations on the relation of the ADRENAL glands to the blood pressure response during cerebral anaemia in cats and rabbits. Coombs (Helen) & Rogoff (J. M.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 41-43.

In cerebral anemia repeated short occlusions of the head arteries may result in a change of the typical curve of blood pressure usually produced by cerebral anemia. There are two distinct parts to this modified curve. Winkin has suggested that some product of adrenal activity is responsible for the second part of the rise. The authors have tested this by using cats and rabbits in which the adrenals were tied off or excised. The absence of all secretion does not modify the curve. The number of blood pressure responses to cerebral anemia that can be produced is dependent largely on the general blood pressure in the animal at the time the arteries are occluded.—J. C. D.

Malignant hypernephroma of the right ADRENAL (Malignes Hypernephrom der rechten Nebenniere). Fraenkel (E.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1370.

Case report of a girl of 9 with a beard, much hair on the trunk, a great deal on the pubes and a very large clitoris. Postmortem examination showed that there was hypernephroma of the right adrenal, with hyperplasia of the left. In the large ovaries scarcely any follicles were found.—J. K.

(ADRENALS) Paroxysmal tachycardia and melanodermia of Addison type. Sympathicotonic pathogenesis (Tachycardie paroxystique et mélanodermie du type Addisonien. Leur pathogénie sympathicotonique). Gilbert (A.) & Coury (A.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1596-1609.

Studies in fatigue. XII. The effect of ADRENAL secretion on non-fatigued and fatigued skeletal muscle. Gruber (C. M.), Am. J. Physiol. (Balt.), 1922, **62**, 438-441.

"Adrenal secretion evoked by splanchnic stimulation increases the height of muscular contraction of both the non-fatigued and fatigued skeletal muscle." It therefore cannot be regarded as a specific antagonist to the so-called fatigue substances.—T. C. B.

The ADRENALS and anaphylaxis (Surrénales et anaphylaxie). Képinow (L.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 327-329.

Having studied the rôle of the **thyroid** in anaphylaxis, the adrenals have been studied in the same manner. The removal of the major part of the suprarenals does not prevent shock when sensitizing injection is made after the operation; on the contrary, guinea pigs show a much greater sensibility to the intoxicating dose than do the normal controls. This increased sensibility does not manifest itself in passive anaphylaxis.—T. C. B.

Influence of various conditions on the ADRENAL vessels. Masuda (T.), Acta scholae med. univ. imp. (Kioto), 1922, **5**, 57-74; abst., Physiol. Abst., 1922, **1**, 506.

Adrenaline (1 to 10,000-50,000) constricts, and lower concentrations have no effect when perfused through the adrenals.—R. G. H.

ADRENAL tumor (Tumor der Nebenniere). Melchior, Klin. Wchnschr. (Berl.), 1922, **1**, 2115.

ADRENALS and PANCREAS antagonism (Sull' antagonismo fra surrenali e pancreas). Moscato (G.), Folia med. (Napoli), 1922, **8**, 353-366.

The adrenals of normal dogs 3 or 4 kg. in weight contain about 1 mg. of adrenalin. After ablation of the pancreas and succeeding experimental diabetes there is an increase in the size of the adrenals, which contain as much as 4 mg. of adrenalin; this is lost in 14-24 days after the operation. Thus it is shown that at first decreased pancreatic function causes increased adrenal function, but that later, due to lack of stimulation from the pancreatic hormone, the adrenals function less than normal.—G. C.

(ADRENALS) Addison's disease and pigmentary cirrhosis (Maladie d'Addison et cirrhose pigmentaire). Oddo (C.) & Oddo (J.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1578-1581.

(ADRENALS) On the experimental basis of the theory of gangraena arteriitica SUPERENALIS. Oppel (V. A.), Lancet (Lond.), 1922, **ii**, 116-121.

The following criticisms of the theory of the cause of spontaneous gangrene have been given in a previous communication. In the coagulation of the blood certain protein-forming amines are

formed possessing vasoconstricting powers and therefore the vaso-constricting effects of the serum may be ascribed, not to adrenaline, but to amines. In the blood plasma from such cases it has never been possible to prove that the vaso-constricting substance was adrenaline. Adrenaline is a substance that breaks up so rapidly that it is not found in the peripheral vessels. Oppel answers these criticisms as follows. The blood serum of spontaneous gangrene cases is richer in vaso-constricting substances than normal serum; whether it is due to adrenaline or not has not been shown. The degree of dilution of the plasma—500 times—used in the laboratory investigations and the degree of sensitiveness of the analyzing apparatus are the causes of the negative results. The separated ear of the rabbit and the separated human finger are not sufficiently sensitive to physiological quantities of adrenaline because of the initial spasm of the arterial walls. In the separated fingers 1 in 50,000,000 solution of adrenaline produced no vasoconstrictor effect. Very approximate estimates of adrenalin in the blood are dilutions of 1:3,000,000,000 to 1:15,000,000,000. Further the isolated ear of the rabbit is complicated by oedema of the tissues, which also obscures the reaction. As to the duration of adrenaline in the circulating blood, the shortest period for its breaking up is 30 seconds, which is about half the circulation time, hence it can not fail to reach the peripheral vessels. In some personal experiments on rabbits, the femoral or axillary artery was tied and 1 or 2 cc. of 1 in 10,000,000 or 20,000,000 solution of adrenaline in Locke's solution was injected into the distal end of the artery. When the rabbit was freed there was a delay in the movements of the foot with contractures of the extensor group of muscles. With the stronger solutions there was complete paralysis of the wrist which wore off in about 3 hours. Controls with ligation and injection of Locke's solution gave no such reaction. It is estimated that the dilution of adrenaline in the peripheral vessel after mixing with the blood is 1 in 40,000,000 to 80,000,000. This indicates that living tissue reacts more energetically to adrenaline than separated ears or fingers.—R. E. K.

(ADRENALS) Diagnosis of Addison's disease (Le diagnostic de la maladie d'Addison). Sézary (A.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1572-1575.

The statement is made that any asthenia which is not accompanied by an abnormal rapid muscular weakness is not of adrenal origin.—F. S. H.

(ADRENALS) Diagnosis of Addison's disease (Le diagnostic de la maladie d'Addison). Sergent (E.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1679.

The supposed relation of the ADRENALS to reflex volume changes in the denervated limb. Stewart (G. N.) & Rogoff (J. M.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 36-37.

When the central end of a peripheral nerve is stimulated the volume of the hind limb, previously denervated by section of the anterior crural and sciatic nerves, increases coincidently with the rise in blood pressure, and then diminishes to less than the initial volume. Bayless explains this as a reaction of the muscular coat of the arteries to stretching. Von Anrep claims that it is due to increased output of adrenin. The authors get the reaction in dogs after the adrenals have been removed. While not excluding adrenin as a factor, they conclude it is not a necessary one for this reaction and that Bayless' explanation is satisfactory.—J. C. D.

Histopathology of the ADRENAL capsules in various nervous and mental diseases. (Contribution à l'histopathologie des capsules surrénales dans les diverses maladies nerveuses et psychiques). Vasilesco (C.), Bull. et mém. Soc. de neurol., psychiat. et psychol. de Jassy, 1922, **3**, 41-44 (January).

Lipoids are found in large amounts in the adrenal cortex in cases of senile dementia, nephritis, tuberculosis, meningitis, mongolism, melancholia, and general paralysis. A little less is present in cases of epilepsy, dementia precox, and pellagra. The glomerular zone seems particularly well supplied in manic depressive psychosis and hydrocephalus. Sclerous tissue is found in pellagra, general paralysis, melancholia and senile dementia. Adenomas were found in manic-depressive psychosis, mongolism and general paralysis. Cortical hyperplasia was found in dementia precox, epilepsy, general paralysis and hydrocephalus. The medullary substance was very much reduced in the cases of melancholia.—F. S. H.

(GONADS) Relation of the female sex glands to the ADRENALS and THYMUS (Uber Beziehungen der weiblichen Keimdrüsen zu Nebennieren und Thymus). Walter (H.), Frankfurt Ztschr. f. Path. (Weisb.), 1922, **27**, 276-289.

The paper consists of an analysis of the autopsy findings in 61 females varying in age from a few days to 83 years. In comparing the body weight and length with the weights of the suprarenals, ovaries and thymus the author found that old age and chronic cachectic diseases induced ovarian atrophy but has no notable influence on the weight of the suprarenals. He observed that in sexually mature individuals with persistent thymus the ovaries were quite large even when the suprarenals were not hypoplastic. No parallelism between the fat content of the ovaries and the suprarenals was noted.—H. L. J. (D. M.)

The ADRENALS and cortical epilepsy (Surrénales et épilepsie corticale). Wertheimer (E.) & Dubois (C.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 301-303.

H. Fischer asserts that following ablation of the suprarenals in rabbits convulsive substances (amyl nitrite) and cortical excitation, even by strong currents, no longer cause convulsions. The observations were repeated on dogs, as rabbits are known to be refractory to cortical epilepsy. After suprarenal ablation in dogs, cortical excitation is followed by the same tonic and clonic spasms of the muscles, with the other symptoms accompanying epilepsy of this type in intact animals. Experiments are described, and the tone of the article is critical.—T. C. B.

The beginning of function in the SUPRARENAL medulla of pig embryos. Weymann (M. F.), Anat. Record (Phila.), 1922, **24**, 299-313.

The chromaffin reaction first appears in embryos having a length of 40 mm. At first it is faint and does not occur in all cells of the medulla. By 75 mm. all such cells show the reaction.—W. J. A.

The influence of d-, l-, and dl-ADRENALINE on beating and not-beating heart-strips [Das Verhalten des Herzstreifenpräparates (nach Loewe) unter verschiedenen Bedingungen. II. Versuche über den Einfluss von l-, d-, und dl-Adrenalin auf den schlagenden und nichtschlagenden Herzstreifen]. Abderhalden (E.) & Gellhorn (E.), Arch. f. d. ges. Physiol. (Berl.), 1922, **196**, 608-628.

The limiting concentrations producing action on the beating heart-strip of the frog are: l-adrenaline 1:15 million, dl-adrenaline 1:7.5 million, d-adrenaline 1:1.5 million. At the limiting or slightly higher concentrations the action is very transitory, but lasts longer with increased concentration; the duration of action is less with d- than with l-adrenaline. In high concentrations both produce, besides the increase of contraction, a slowing. Higher concentrations are required to stimulate the automaticity of a not-beating than of a beating strip.—A. T. C.

A comparison of the atheromatous action of organic and synthetic ADRENIN (Action athéromatogène comparée des adrénalines organiques et synthétiques). Arloing & Thévenot, XVI Congr. franç. de méd. (Par.), 1922, Oct. 12-14; abst., Presse méd. (Par.), 1922, **30**, 926.

After the injection in rabbits of 12 drops, given in 5 doses over a period of 24 days, or of 10 drops, given in 4 doses over a period of 28 days, the authors found that synthetic, levogyric adrenin, more hypertensive than racemic adrenin, caused more atheroma, and also

that it was twice as atheromatogenous as organic adrenin. They conclude, therefore, that the atheromatous effects are not in direct relation with the hypertensive, vasomotor effects, since two adrenins, having identical action on the vasoconstrictors, differ so profoundly in their toxic effects on the aorta of the rabbit.—R. G. H.

Glandular physiology. LIV. Leon Asher. Demonstration of ADRENALIN in arterial blood (Beiträge zum Nachweis von Adrenalin in arteriellern Blut der Tiere). Asher (L.) & Schneider (C.), Biochem. Ztschr. (Berl.), 1922, **133**, 373-390.

Rabbits were used in these experiments. The superior cervical ganglion of one side was extirpated. The injection of strychnine into the otherwise uninjured animal produced marked pupillary dilation on the side of the operation and only minor similar reaction on the normal side. After the splanchnic nerves had been extirpated on both sides, the pupillary reaction to strychnine could not be produced. The latter phenomenon is attributed to a lack of increased adrenalin secretion following the strychnine stimulation of the splanchnics, and as a proof of the presence of adrenalin in the major circulation under normal conditions.—F. S. H.

Death by ADRENALIN in the course of chloroform anesthesia. Cardiac syncope (De la mort par l'adrénaline au cour de l'anesthésie chloroformique. Synope cardiaque). Bardier (E.) & Stillmunkes (A.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 321-324.

The death of chloroformed animals following injection of about 0.01 mg. of adrenalin per kg. body weight is the result of cardiac syncope accompanied by fibrillation, as established by Levy in 1911. It consists in intoxication of the myocardium. It resembles the ordinary chloroform syncope, but its mechanism appears to be different.—T. C. B.

Calcium salts and ADRENALIN in the treatment of fractures (Sali di calcio ed adrenalina nella cura delle fratture). Battaglia (M.), Rassegna Internaz. di clin. e terap. (Napoli), 1922, **3**, 459-460 (October).

The author has obtained good result in the treatment of fractures—whether open or closed—by adding to the usual treatment adrenalin 10 drops 1:1000 and 10 cgm. calcium phosphate twice a day. The treatment proved efficacious in the formation of normal callous as well as in offsetting the effects of nervous traumatism. The author attempts no explanation except to advance the theory that adrenalin mobilizes the calcium salts in the organism.—J. V.

Thermo-electric studies of temperature variations in animal tissues. III. ADRENALIN. Crile (G. W.) & Rowland (Amy F.), **Am. J. Physiol. (Balt.), 1922, 62, 370-382.**

By means of a specially devised thermo-couple, temperature changes in the brain and other organs under various conditions were observed. The response of the brain to injections of adrenalin was so uniform as to justify a separate report. The temperature of the brain and thyroid was increased by adrenalin. The liver and voluntary muscles were not affected. In the absence of the liver adrenalin produced no change or a diminished temperature. There was no reaction after thyroidectomy. Under ether the reaction of the brain was greater than in normal animals; under nitrous oxide, less. Many charts are included.—T. C. B.

The blood picture after injection of ADRENIN in blood diseases (Das Adrenalinblutbild bei Erkrankungen der hämopoetischen Organe). Hittmair (A.), Ztschr. f. klin. Med. (Berl.), 1922, **95**, 366-383.

Changes after injection of adrenin are not typical and do not enable diagnosis of special changes in the function of organs or tissues of the body. The injection of 1 mg. may be followed by the occurrence of pathological blood cells in the blood stream, but this cannot be considered as proof of an increased formation of blood cells. They are found only when they are previously on the point of coming into the blood.—J. K.

The rôle of ADRENALIN in the hypertension produced by exciting the splanchnic nerve (Nouvelles expériences sur le rôle de l'adrénaline dans l'hypertension produite en excitant le nerf splanchnique). Houssay (B. A.) & Marconi (A. P.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 1049-1052.

To answer the objection of Stewart and Rogoff, the circulation in dogs was reduced to the head, thorax, anterior extremities, suprarenals and one posterior foot by suitable ligatures. Under these conditions stimulation of the splanchnic causes an elevation of pressure and at the same time the denervated hind foot diminishes in volume. If the lumbo-capsular vein is occluded, no such change occurs. The authors conclude that excitation of the splanchnic causes an adrenal discharge.—T. C. B.

The rôle of acid in ADRENALIN hyperglycemia (Ueber die Rolle der Säurewirkung beim Zustande kommende Adrenalinhyperglykämie). Kornfeld (F.) & Elias (H.), Biochem. Ztschr. (Berl.), 1922, **132**, 192-211.

Subcutaneous injections of adrenalin in rabbits induce hypocapnia of some hours duration. This phenomenon is not produced in dogs. When man is similarly treated there occurs either no reaction or, more frequently, a minor lowering of the CO_2 tension of the alveolar air and it is of short duration. Hypocapnia, therefore, is not an essential preliminary for adrenalin hyperglycemia.

The question as to whether a local acidification of the liver is of significance in adrenalin hyperglycemia was not answered by these studies.—F. S. H.

Studies of Graves' syndrome and the involuntary nervous system. IV. The vascular response of the pithed cat to single intravenous injections of ADRENALIN. V. The vascular responses of the pithed cat to repeated intravenous injections of equal doses of ADRENALIN. VI. Attempts to alter the vascular response of the pithed cat to repeated injections of similar doses of ADRENALIN. VII. On the mechanism of sensitization to subcutaneous injections of ADRENALIN. Lieb (C. C.) & Hyman (H. T.), Am. J. Physiol. (Balt.), 1922, **63**, 60-93.

Papers I and II of this series will appear in Am. J. M. Sc., paper III in the Arch Int. Med. early in 1923. Papers VIII and IX have appeared in the J. Am. M. Ass., 1922, **79**, 1099; 1213. In the present papers the vascular response of the pithed cat to adrenalin has been taken as a satisfactory index of the functional state of the myoneural junctions of the involuntary nervous system. Pithing was considered incomplete if the blood pressure was higher than 50 mm. hg. or if it varied spontaneously 15 per cent. The response to a single intravenous injection is analyzed and its latent period, ascending and descending limbs and fastigium are discussed. In fatigue the reaction is of longer duration and the return to normal delayed, showing that sensitiveness to adrenalin accompanies atony rather than tonicity of the thoracico-lumbar division. In the vascular response to repeated injections there is a constant variable when all known variables are controlled. It consists of a progressively increasing response and has been called "sensitization"; it is necessary to eliminate this "sensitization" before factors that alter adrenalin response can be given their true value. Before a substance can decrease adrenalin response it must overcome the sensitization effects; of all substances tried, Mg. alone showed a specific diminution of response. Sensitization is probably due to an alteration in the peripheral structures of the involuntary nervous system. The first subcutaneous injection of adrenalin has no effect, but succeeding injections may give a clear-cut sensitizing reaction. The mechanism is probably the same as for intravenous injections and as in the latter is independent of the thyroid. There is no scientific basis for the value of the Goetsch test.—T. C. B.

The influence of ADRENALIN on metabolism in various excised tissues. Martin (E. G.) & Armitstead (R. B.), Am. J. Physiol. (Balt.), 1922, **62**, 488-495.

The addition of adrenalin to the solution results in an augmentation of the production of CO_2 in frog's muscle. In the present paper, it is shown that this is not specific. Frog's brain, mesone-

phros, liver, stomach tissue and intestinal tissue, all show a two- or three-fold augmentation of acid production in the presence of adrenalin.—T. C. B.

ADRENALIN in weak heart action (Insufficiencia cardiaca e adrenalina). Moreira (da F. J.), Arch. brasil. de med. (Rio de Jan.), 1921, **11**, 1-10.

As regards the neurogenic or myogenic origin of asystole a great deal of importance must be accorded to hormone insufficiency (adrenalin, hypophysis). The author has obtained amelioration of symptoms in severe asystole by the injection of 0.5 mg. of adrenalin.

—B. A. H.

The passage of ADRENALIN from the cerebrospinal fluid into the general circulation (Le pasage de l'adrénaline du liquide céphalorachidien dans la circulation générale). Nitzescu (I. I.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 818-820.

Results of the passage of adrenalin from the cerebrospinal fluid into the general circulation, usually determined by its effect on blood pressure, have been divergent. The author observed the changes in blood sugar and in the leucocyte picture. Dogs were injected without anesthesia into the subarachnoid space, traversing the atlanto-occipital membrane, and fluid was withdrawn equal to the amount of solution injected. Such injections were followed by an increase of blood sugar, and leucocytosis, and it was concluded that adrenalin passed into the circulation from the cerebrospinal fluid, but its passage was so slow that it had no appreciable effect on blood pressure.—T. C. B.

(ADRENALIN) Vasodilator mechanisms. III. The action of nicotine. Ranson (S. W.) & Wightman (W. D.), Am. J. Physiol. (Balt.), 1922, **62**, 405-415.

Of endocrine interest in that after nicotine has paralyzed the dilator mechanism adrenalin still produces its characteristic vascular changes.—T. C. B.

Comparative pressor power of racemic and laevo ADRENALINE. Richaud (A.), J. de pharm. et chim. (Par.), 1922, **26**, 81-86.

Racemic adrenaline employed in small doses of the order of 0.01 mg. increases the blood pressure to a somewhat less degree than laevo adrenaline, but the difference is not great, but varies from 10 to 15% in general, although it may be as much as 25 to 30%. As the dose is increased to 0.04 to 0.05 mg. the difference in activity disappears, and as the usual therapeutic dose is 0.04 to 0.1 mg. there is no disadvantage attendant on the use of the racemic compound.—Physiol. Abst., **7**, 448.

(ADRENIN) Barium-epinephrin antagonism on the excised surviving intestine. Roth (G. B.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 43.

This antagonism, previously reported by the author in frog's intestine, can likewise be demonstrated with strips of intestine from the rabbit and turtle.—J. C. D.

The technic of ADRENALIN studies in man (Zur Methodik der Adrenalinuntersuchungen am Menschen). Rothmann (M.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 936-937.

The author discusses the reasons for different authors observing different effects from the injection of adrenaline. To obtain uniform results three conditions are necessary. The subject must be in such a state of mind that the adrenalin has no influence on psychical functions (in man injection of scopolamin-morphin generally secures this). Adrenalin must be injected intravenously; this is quite harmless when such amounts as 0.1 mg. are slowly injected. The blood pressure must be measured with an exact instrument. The apparatus of Riva-Rocci, which is ordinarily used for this kind of work, is not exact enough. If these precautions are taken the first effect of an injection is decreased pulse rate with a rise of blood pressure. An increased pulse rate shows that psychical processes have changed the effect of adrenalin.—J. K.

Further experiments on ADRENALIN (Weitere Untersuchungen über Adrenalin). Stuber, Ruszman & Proebsting, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1568.

See Endocrin., **6**, 671.

Melanins of ADRENIN origin (Melanine di origine adrenalinica), (Ueber Melanine, die aus Adrenalin hervorgehen). Saccardi (P.), Arch. di fisiol. (Florence), 1922, **20**, 205-208; also Biochem. Ztschr. (Berl.), 1922, **132**, 439-442.

Concentrated chlorine-water was added to 300 grams of official adrenaline-hydrochloride (Givandan and Laverotte). From this solution, changing to rose-red, then yellow, a colloidal brown solution was obtained after 24 hours, from which, when acidified with hydrochloric acid and evaporated on the water-bath, black flecks (0.25 gram) separated. (The Parke-Davis preparation gave no colloidal solution but a black precipitate after 24 hours.) The amorphous black substance was soluble in water, and two-thirds soluble in 95% alcohol, the soluble portion giving reactions similar to the natural melanins and the "pyrrol-black" of Angeli.—A. T. C.

(ADRENIN) Lactic acid formation after sugar puncture (Zur Frage der Milchsäurebildung nach Zuckerstich). Sammartino (V.), Biochem. Ztschr. (Berl.), 1922, **132**, 215-217.

Piqûre of rabbits is followed by an increase in the lactic acid content of the liver, but not to so great an extent as that following adrenalin administration.—F. S. H.

Action of ADRENALIN on the change during alimentation and fasting (Azione dell'adrenalina sul ricambio durante l'alimentazione e nel digiuno). Susanna (V.), Folia med. (Napoli), 1922, **8**, 234-244.

Dogs were experimented on. The results were doubtful, but in general it appeared that elimination of nitrogen and of the salts diminished during alimentation when adrenalin was administered. The contrary was due during fasting.—G. C.

Physiological ADRENALINEMIA (Existe-t-il une adrénalémie physiologique?). Tournade (A.), J. de méd. et de chirurg. de l'Afrique du Nord, 1922.

If cross-circulation is made between the suprarenal vein of one dog and the jugular of a second, then after stimulation of the splanchnic in the first all the adrenaline effects (raising of blood pressure, etc.) result. Doubt thrown on the theory of hypo- and hyper-glycemia by the negative results obtained by simple injection of blood from a stimulated dog is thus not justified.

—Physiol. Abst., **7**, 447.

Intravenous infusion of normosal and ADRENIN in collapse caused by peritonitis or after operations (Die intravenöse Dauertropfinfusion mit Normosal und Adrenalin zur Behandlung des peritonisischen und postoperativen Collapses). Wiedkopf (O.) & Hilgenberg (F. C.), Beitr. z. klin. Chir. (Tübing.), 1922, **127**, 229-237.

The authors recommend in collapse continuous intravenous infusions of normosal (a kind of Ringer's solution) containing 1 cc. 1% adrenin per L. Forty to 60 drops should enter per minute. In very severe cases the first half liter is given quickly. Two and a half to 4 liters are given daily. Quick improvement of the pulse rate is the first symptom of success. Prognosis is best when micturition remains normal.—J. K.

(ADRENIN) Effects of transfusion of carotid blood taken during splanchnic excitation (Effets de la transfusion de sang carotidien recueilli pendant l'excitation du splanchnique). Zunz (E.) & Govaerts (P.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 881-882.

The authors tried to show the presence of adrenalin in the blood after stimulation of the splanchnics, by a crossed transfusion in dogs. Their results were negative.—T. C. B.

(AUTONOMIC NERV. SYST.) Pathology of the sympathetic. Brown (W. L.), Encéphale (Par.), 1922, **17**, 473-485 (October).

Brown emphasizes the essentially defensive role of the sympathetic nervous system. It sends the flood of energy toward the exterior, while the parasympathetic nervous system sends it inward. The sympathetic functions in the plane of the subconscious. Pain, fear and anger are the special stimuli which rouse it to action, and when the adequate motor reaction is prevented or restrained, the preparations for defense are thus diverted from their natural purpose and may display a pathologic character of perseveration or dissociation. The restraints of civilization are liable to entail this perversion of a primary defensive mechanism, and this, he reiterates, is the key to the general pathology of the sympathetic nervous system. Among the instances he cites are the almost epidemic appearance of **hyperthyroidism** after the San Francisco earthquake, after the massacres at Kishineff and during the period of airplane bombing of London. He adds that as the sympathetic is the intermediator between the skin and the endocrine glands and the brain, this explains how the effect of climate on the skin can modify brain functioning. Certain associations of ideas can act on the autonomic nervous system independently of the will. Hence if we can realize this association of ideas voluntarily, the same autonomic reactions may follow.—J. Am. M. Ass., **79**, 1961.

(AUTONOMIC NERV. SYST.) Methylene blue, antagonistic to excitants of the PARASYMPATHETICS (Le Bleu méthalène, antagoniste des excitants parasympathetiques). Heymans (C.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 396-398.

Experiments on the hearts of frogs, turtles and dogs demonstrate that methylene blue possesses, although to a less degree than atropine, an action antagonistic to that of muscarine, acetylcholine and arecaline; the action is reciprocal to a certain degree.—T. C. B.

Tumors of the CAROTID GLAND (Gezwellen der glandula carotica). Nieuwenhuijse, Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, **66**, (II), 2024-2025.

Treatment of DIABETES (Diabetes-Therapie). Assmann, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1665; Klin. Wchnschr. (Berl.), 1922, **1**, 2069.

The author recommends treatment of diabetes by restriction of diet, the value of which was proved by the war.—J. K.

The effect of INSULIN on experimental hyperglycemia in rabbits. Banting (F. G.), Best (C. H.), Collip (J. B.), Macleod (J. J. R.) & Noble (E. C.), Am. J. Physiol. (Balt.), 1922, **62**, 559-580.

"The present investigation was undertaken to obtain further evidence of the scope of the action of insulin by studying its effect on the various experimental conditions that are known to cause marked hyperglycemia in rabbits." The rabbits were of uniform size and breed, and fed several days preceding the experiments on oats and hay, sometimes with sugar added. Blood was taken from the ear and sugar determined by the Schaffer-Hartman method. When the fall in blood sugar was established by injections of insulin, piqûre, epinephrin, ether, asphyxia (mechanical or CO) did not cause the usual degree of hyperglycemia; there was sometimes a rise, but not to the level obtaining before insulin was given. Even when insulin was given at the time of experiment, hyperglycemia did not occur, or was greatly diminished.—T. C. B.

Islands of Langerhans free in the connective tissue of an otherwise normal human PANCREAS (Über frei im Bindegewebe liegende Langerhans'sche Zellhaufen in einem sonst normalen menschlichen Pankreas). Clara (M.), Anat. Anz. (Jena), 1922, **55**, 402-406.

The islands described were found free in the connective tissue of the pancreas, unassociated with the usual parenchyma. In one instance an island was connected to an excretory duct. Independent ducts were frequently seen in the neighborhood of these islands. One interpretation of this unusual condition is that local atrophy of the alveolar parenchyma had occurred, with a persistence of the islands and some of the ducts.—A. T. R.

Influence of PANCREATIC perfusate upon the carbohydrate metabolism of depancreatized animals. Clough (D. C.), Stokes (A. M.), Gibbs (C. B. F.), Stone (N. C.) & Murlin (J. R.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 66-67.

After removal of the pancreas in cats and dogs, results typical of diabetes were obtained. The respiratory quotient, blood sugar, and D/N ratio were studied. Sugar, in the form of dextrose or sucrose, was given through a stomach tube. Pancreatic perfusate was then administered intravenously, subcutaneously, or intraperitoneally. This perfusate was obtained from the pancreases of cats, dogs, pigs, or oxen. There followed a rise in the respiratory quotient, a marked drop in the level of the blood sugar and changes in the D/N ratio. The report contains an outline of the exact methods used.—J. C. D.

Acetone forming microorganisms in the intestinal flora of DIABETICS (Sur la présence de microbes acétonogènes dans la flore intestinale des diabétiques). Berthelot (A.) & St. Danysz-Michel, Compt. rend. Acad. d. sc. (Par.), 1922, **174**, 1303-1306; abst.. Ber. u. d. ges. Physiol. (Berl.), 1922, **14**, 274.

Acetone forming microorganisms are rather widely distributed. None was found in the stools of 32 persons who were either healthy or suffering from conditions other than diabetes. In the stools of 22 persons with diabetes of varying degrees of severity, such bacteria occurred in 17 cases. The organisms are not of any single type, but include bacilli, cocci, and others. Many are spore forming; all are highly resistant to acetone. The occurrence of these organisms in diabetics is probably dependent upon the presence of undigested glucose in the intestine. A few of the organisms, when given daily to rabbits, in massive doses, cause glycosuria; others do not.

—E. C. A.

DIABETES, Beta-oxybutyric acid and levulose (Diabéte, acide B-oxybutyrique et lévulose). Desgrez (A.), Bierry (H.) & Rathery (F.), Compt. rend. Acad. d. sc. (Par.), 1922, **175**, 536-539 (September).

Different sugars are not interchangeable in nutrition. There is a chemical alimentary specificity. Fructose remedies certain metabolic accidents, and in diabetes combats the elimination of oxybutyric acid. When the sugar tolerance of a diabetic is established, fructose should be the sugar given, plus a due supply of phosphates and vitamin B.—Physiol. Abst., **7**, 504.

DIABETES MELLITUS together with DIABETES INSIPIDUS (Untersuchungen über einen Fall von gliechzeitig bestehenden Diabetes mellitus und insipidus). Freund (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 1780-1785.

The patient was a man of 36 who had always suffered from polydipsia. His urine was repeatedly analyzed but no sugar was detected until he was 34 years old. He died in coma. Postmorten examination showed that the **hypophysis** was small and that the veins of the pars anterior were much congested. No other changes were found macroscopically or microscopically. The "thirst test" and the "pituglandol test" gave results typical of diabetes insipidus, but the extraordinary thirst did not disappear, as is usually the case, when pituglandol was injected. The author believes that it is possible that the primary cause of both types of diabetes is situated in the **pancreas** and quotes the results of many authors who, by lesions of the pancreas, obtained polyuria without glycosuria. There may be an important relationship between the hypophysis and the pancreas. It is more probable, however, that pathological changes simultaneously affect the centers of water and sugar metabolism which are situated near each other in the interbrain.—J. K.

Calcium change in DIABETES (Contributo allo studio del ricambio del calcio nel diabete). Galdi (G. F.) & Paxeddu (G. E.), Folia med. (Napoli), 1922, **8**, 68-77; 109-120.

Thermal stations and "modern treatment" of DIABETES (Stazioni termali e "trattamento moderno" del diabete). Monod (G.), Arch. med. Hydrol., No. 1 (May); abst., Rassegna internaz. di clin. e terap. (Napoli), 1922, **3**, 470-471.

The influence of PANCREATIC extracts upon the carbohydrate metabolism of depancreatized dogs. Gibbs (C. B. F.), Clough (H. D.), Stone (N. C.) & Murlin (J. R.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 67-68.

The experiments were similar to those given above (Clough et al.), except that an extract of freshly removed dogs' pancreas was used. Extracts given by stomach had very little effect. Intravenous, intraperitoneal, intramuscular, and subcutaneous injections resulted in a marked fall of blood sugar level, the lowest level occurring about 4 hours after the injection, regardless of the route used. The subcutaneous injection method was least harmful to the animal as a whole and proper purification of the extract did away with most of the painful effects at the place of injection.—J. C. D.

Treatment of DIABETES MELLITUS (Behandeling van diabetes mellitus). Hoogslag (W.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, **66** (II), 871-875.

The modern methods of dietetic treatment are shortly reviewed. —J. K.

Two hundred and fifty cases of DIABETES (Opmerkingen naar aanterding van 250 gevallen van suikerziehte). Hoogslag (W.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, **66**, (II), 1934-1951.

A collection of important practical observations—J. K.

Is the yeast treatment of DIABETES logical [Ist die Gegründung der Wirkung der Ferment (Hefe) therapie bei Diabetes mellitus zutreffend]? Lenné, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1310-1311.

Some investigators recommend the administration of yeast in diabetes. Lenné thinks this is not logical.—J. K.

(DIABETES) Properties and methods of preparation of the ANTI-DIABETIC substance (glucopyron) generated by the PANCREAS. Murlin (J. R.), Pro. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 70.

The author outlines the essential steps in the preparation of this substance and points out that in alcoholic extracts all the active substance is not found in the final extract. He reviews its physical properties, and calls attention to a paper by Murlin and Kramer,

published in 1916, in which they reported the demonstration of the sugar oxidizing property of aqueous pancreatic extract when given by mouth. He suggests the name, glucopyron, for the active substance however obtained.—J. C. D.

On the relation between ligature of the ductus thoracicus and the tolerance for carbohydrate. Ohara (T.), Tohoku J. Exper. Med. (Sendai), 1922, **3**, 163-176.

There generally results a protracted hyperglycemia, frequently accompanied by glycosuria. The author regards the condition as due to a part of the pancreatic hormone being secreted into the blood stream via the lymph.—Physiol. Abst., **7**, 503.

Prognosis of DIABETIC retinitis as regards life and vision (Le prognostic vital et le prognostic visuel des rétinites des diabètiques). Onfray (R.), Ann. d'ocul. (Par.), 1922, **159**, No. 8 (August); abst., Presse méd. (Par.), 1922, **30**, 859.

Onfray studied 76 new glycosuric subjects with retinitis in addition to the 24 cases already reported by him in the "Ann. d'ocul." in 1918. Among this last group, 7 who died during the first 3 years of his observation had hypertension (maximum 25°, minimum 13°). The patients with well defined Ambard's constant usually survived. True diabetic retinitis did not seem to be so often fatal as the hemorrhagic forms. But prognosis as regards vision is sombre, although complete loss of sight was rare. The visual acuity was so poor in these patients that they could not read, play cards, or even feed themselves.—R. G. H.

Cause and dietetic treatment of severe DIABETES (Zur diätetischen Therapie der schweren Diabetesfälle und zur pathogenetischen Theorie dieser Erkrankung). Petrén (K.), Psychiat. en Neurol. Bl. (Amst.) (Neurotherapie), 1921, 25-77.

In diabetes the reduction of the quantity of protein in the diet is as necessary as the reduction of the carbohydrates. A regulated diet is necessary even when the excretion of nitrogen does not exceed 3 to 4 gms. daily. The diet recommended may be given for a long time (in one case 82 days) without symptoms of underfeeding. The patients may even gain weight. The diet consists only of vegetables, fat and butter and blueberries. The author objects to the Allen treatment because in some cases it may produce acidosis, which may even prove fatal, and because the patients lose not only flesh, but strength and energy. In some cases in which the Allen treatment was used the patients did not die of diabetes but of starvation. Allen has stated that after a certain time in severe diabetes the patients cannot support fat. Petrén believes that this is true only when enormous quantities are given and in the last stage when the patients can support nothing. Neurological symptoms of

diabetes, when treatment is given according to Petrén's method, rapidly disappear. When the knee jerks are negative they do not come back. A fact peculiar to diabetes is that as soon as the quantity of nitrogen that is excreted exceeds a certain amount acidosis begins. Therefore, Petrén's diet, which tends to diminish the excretion of nitrogen, has a splendid effect in acidosis. Another advantage of the recommended diet is that the carbohydrate tolerance may be increased. Even with this diet, however, the prognosis of diabetes remains as bad as before.—J. K.

Los regímentes equilibrados en la DIABETES. Rathery (F.), Arch. de med., cirug. y espec. (Madrid), 1922, **9**, 289-294 (November).

A brief general discussion of the factors determining a properly balanced diabetic ration.—R. G. H.

(DIABETES) Relation between the sugar content of blood plasma and cerebro-spinal fluid (Beziehungen zwischen dem Zuckergehalt des Plasmas und des Liquors). Rusznyák (S.) & Csáki (L.), Biochem. Ztschr. (Berl.), 1922, **133**, 355-357.

A series of determinations of the sugar reducing content of blood plasma and cerebro-spinal fluid taken from the same individual at the same time. In both diabetic and non-diabetic subjects the sugar content of the cerebro-spinal fluid is always less than that of the blood plasma, and is about 0.05%. However, it is possible that when sudden changes in blood sugar occur, because of the sluggish change in cerebro-spinal fluid, higher values may be found in the former than in the latter.—F. S. H.

Three months study of the influence of the anti-diabetic substance on a case of severe DIABETES. Sutter (C. C.) & Murlin (J. R.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 68-69.

Anti-diabetic substance was given through a duodenal tube with good results. At the end of a week the treatment was stopped for three weeks. The blood sugar rose, but not to its previous level. Treatment was resumed in the form of 45 subcutaneous injections continued over a period of 2 months. The blood sugar was kept down, and the sugar, acetone, and diacetic acid disappeared from the urine and did not reappear again when the diet was made more liberal. Administration by mouth was without results. There was little difficulty experienced with the subcutaneous method. Only 3 of the injections gave any definite local reaction.—J. C. D.

Development of real DIABETES from cholelithiasis via the PANCREAS (Entwicklung eines echten Diabetes aus einer Cholelithiasis auf dem Weg über das Pankreas). Umber, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1221.

The patient first suffered from cholelithiasis. The urine was sugar free even after ingestion of 100 gm. of glucose. There was no hyperglycemia. A tumor began suddenly to grow in the abdomen with symptoms of a disease of the pancreas. There was no glycosuria and no hyperglycemia. An operation was performed upon the pancreas cyst and gall bladder. About 3 months later the patient complained of thirst and itching. Typical diabetes was found.—J. K.

(ENDOCRINE) The influence of substances from yeast cells and organs on the rapidity of decomposition of substances by polypeptidases, carbohydrases and esterases (Untersuchungen über den Einflusz von aus Hefezellen und Organen gewonnenen Stoffen auf den zeitlichen Verlauf der Spaltung von Substraten durch Polypeptidasen, Karbohydrasen und Esterasen). Abderhalden (E.) & Wertheimer (E.), Fermentforsch. (Leipz.), 1922, **6**, 1-26.

Abderhalden prepared from yeast a substance which influences the velocity of alcoholic fermentation. He experimented on the influence of the same substance on the velocity of the decomposition of dipeptids. Optones from the **hypophysis, testicles, ovaries** and **corpus luteum,** cholin and **adrenalin** did not influence the reaction. Optones from the placenta slightly, and from the **thyroid** and **thymus** markedly, increased the velocity. The optones from the thymus and thyroid lost their activity after boiling for 20 minutes. When these optones were dialyzed they were separated into two inactive parts, which, when put together, showed their original activity. That part of the optones which dialyzed was not inactivated by the heat; the other part, which was not dialyzable, was destroyed by heat.—J. K.

A case of Recklinghausen's disease with ENDOCRINE complications (Un caso de enfermedad de Recklinghausen con trastornos endocrinos). Andueza (P.), Med. ibera (Madrid), 1922, No. 256, 241-243.

In many cases of Recklinghausen's disease, endocrine complications may be observed, especially **thyroid** and **suprarenal** insufficiency. According to Revilliod, Castellino, Pende and Chaufard, etc., opotherapy plays an important part in the treatment of this disease. The author describes the case of a cretin in whom neurofibromatosis was present in the region of the thyroid. In addition to the symptomatology proper to cretinism, there were many small tumors and irregularly distributed pigmentation. Histological study of one of the tumors showed it to be a fibroma. Thyroid opotherapy was instituted. In ten months the endocrine complications were much relieved and the small tumors underwent slow regression, many of them disappearing, while those that remained became much smaller in size.—E. B.

Progressive myopia and ENDOCRINE disturbances (Miopias progresivas y pertubaciones endocrinas. Contribución a su estudio etiopatogénico). Argañaraz (R.), Semana méd. (Buenos Aires), 1922, **29**, 1161.

Ectasis of the posterior (myopia), or of the anterior segment (keratoconus), of the eye is observed at the time of greatest endocrine activity. The subjects present a pluriglandular syndrome and are heredosyphilitics.—B. A. H.

ENDOCRINIDES syphilitiques angio-neurotiques et angio-neurotrophiques. Audry & Chatellier, Ann. de dermat. et syph. (Par.), 1922, **3**, June; abst., Presse méd. (Par.), 1922, **30**, 761.

Under the name of "endocrinides syphilitiques" the authors consider those lesions which present no specific structure, which are not dependent upon any one factor, which are not always cured by specific treatment, which are not even specific in the sense that their complex symptomatology depends upon a change which can be determined by any agent except spirocheta. The authors consider Raynaud's disease as an example of "endocrinide syphilitique angioneurotrophique"; the endocrine glands (**thyroid** and **ovary**), influenced by syphilis, affect the **sympathetic system.** Erythromelia of Pick is, like Raynaud's disease, sometimes of syphilitic origin. However, these two syndromes do not represent pure endocrinopathies; in Raynaud's disease, as in vascular erythromelia and syphiloma, there is also true syphilitic arteritis.—R. G. H.

(ENDOCRINE) Sclerodermia. Bolton (G. C.), Maandbl. v. specialistiche Geneesk. (Amst.), 1922, **5**, 72.

The endocrine organs probably play an important part in the pathogenesis of scleroderma. Often important changes are found in the **thyroid** (atrophy of the complete organ, degeneration of the follicles, etc.). In some cases changes in the **hypophysis** have been found. Though changes in the **adrenals** have not been described, combination of Addison's disease and scleroderma are known. Bolten theorizes to the effect that insufficiency of the chromaffin system with a diminished tonus of the sympathic may be an explanation of scleroderma. The low tonus of the muscles of the blood vessels will cause dilatation of the large vessels, especially the veins in the lungs and abdomen, and these vessels will contain large quantities of blood. This, the author believes, combined with the low blood pressure, produces defective circulation in the periphery of the body. Several French authors (Hallopeau, Brissaud) believe that scleroderma is caused by an anatomical lesion of the sympathic, especially the centers (e. g., the vasomotor center of the floor of the third and fourth ventricles). Bolton believes that this is possible, especially since such tumors could cause a decrease in the production of adrenalin.—J. K.

ENDOCRINE disturbances by thallium (Weitere experimentelle Ergebnisse über endokrine Störungen durch Thallium). Buschke (A.) & Peiser (B.), Klin. Wchnschr. (Berl.), 1922, **1**, 2182-2184.

When thallium is given to tadpoles growth as well as metamorphosis is retarded. When **thymus** is added to the thallium retardation of metamorphosis is almost neutralized, but growth remains retarded. In this way dwarf frogs are formed. Thallium seems to produce only functional changes in the endocrine organs, as even severe changes in growth soon disappear after stopping the administration of this metal.—J. K.

New evidence for sympathetic control of some INTERNAL SECRETIONS. Cannon (W. B.), Am. J. Psychiat. (Balt.), 1922, **2**, 15-30.

An address, in which the author reviews the work done in the Harvard Physiological Laboratory on the innervation of the **adrenal** medulla (see Endocrinol., 1922, **6**, 277), of the **liver** as an organ discharging a cardio-accelerator and a pressor agent (see Endocrinol., 1922, **6**, 554), and of the **thyroid** gland (see Am. J. Physiol., 1922, **60**, 476). The author then discusses the nature and location of the central nervous control of these organs and the application to human beings of the results of studies on lower animals. He also considers the bearings of these considerations on the character of emotional reactions.—Author's Abst.

Physical therapy in the light of ENDOCRINOLOGY. Chelmonski (A.), Polska Gaz. Lekarska (Lemberg), 1922, **1**, 534 (June); cit., J. Am. M. Ass. (Chicago), **79**, 1808.

(ENDOCRINE) Pluriglandular thyroid and kidney therapy (Prodotti opoterapici associati). Coronedi (G.), Terapia (Milano), 1921, **11**, 8-12 (March),

A résumé of data indicating a functional relation between the thyroid and the kidney, and supporting the utility of "renothyroid" therapy.—Author's Abst.

(ENDOCRINE) Clinical importance and cause of experimental glycosuria in pregnancy (Ueber den diagnostischen Wert und die Aetiologie der experimentellen Schwangersschaftsglycosurie). Dietrich (H. A.), Klin. Wchnschr. (Berl.), 1922, **1**, 1403-1407.

The Frank-Nothmann test for the diagnosis of pregnancy is positive in 85% of the cases. Since the glucose used by Frank and Nothmann is very expensive, the author recommends the use of artificial honey, which gives the same results. The influence of adrenin on sugar metabolism in pregnancy has been studied, with the conclusion that when the injection of 1 cc. of adrenin 1:1000 is followed by glycosuria pregnancy exists. Dietrich was able to prove that this test is absolutely unreliable. He states that glycosuria in

pregnancy is not renal glycosuria, as real hyperglycemia is always found; it is an alimentary glycosuria with a lowered tolerance for carbohydrates, perhaps caused by the changes during pregnancy in the **hypophysis, liver** and **thyroid.**—J. K.

Functional diagnosis of the diseases of the ENDOCRINE organs (Funktionelle Diagnostik der Erkrankungen des Blutdrüsensystems). Falta (W.), Ztschr. f. ärztl. Fortbild. (Jena), 1922, **19,** 417-427.

A general review.—J. K.

Psychiatry and ENDOCRINE organs (Psychiatrie und innere Sekretion). Fischer (H.), Klin. Wchnschr. (Berl.), 1922, **1,** 2401.

Abstract of lecture.—J. K.

(ENDOCRINE) Methods and purposes of the modern investigations on rickets (Wege und Ziele der neueren Rachitisforschung). Freudenberg (E.), Klin. Wchnschr. (Berl.), 1922, **1,** 1422-1425.

Postulates endocrine deficiency as one cause.—J. K.

El cancer y su origen ENDOCRINICO. Guzman (Z), Prensa méd. argentina (Buenos Aires), 1922, **9,** 175.

It is claimed that cancer may be caused by interruption of endocrine balance.—B. A. H.

(ENDOCRINE) Importance of Abderhalden's reaction in psychiatry (Die Bedeutung der Abderhaldensche Reaktion für Psychiatrie). Kastan (M.), Deutsche med. Wchnschr. (Berl.), 1922, **48,** 1191.

In maniac-depressive psychosis 11% showed a positive reaction of Abderhalden with brain; 14% with **sexual glands.** In dementia praecox, out of 87 cases 27 showed a positive reaction with **thyroid;** 60 with sexual glands; 30 with brain; 12 with the three organs. In epilepsy 33% had a positive reaction with brain. In dementia paralytica 40% had a positive reaction with brain. In some cases of dementia praecox Steinach's **rejuvenation** experiment was tried. The serological reactions remained unaltered by the operation. No clinical details are given.—J. K.

(ENDOCRINE) Active principle of organ extract. Kuboto (S.), Nat. M. J. China (Shanghai), 1922, **8,** 185-191 (September).

Extracts of lung, spleen and **pancreas,** when injected intravenously into the cat, lower the blood pressure. They also cause marked contraction of the isolated uterus of the virgin guinea pig. Both these reactions closely resemble the action of histamine. The author was able to isolate from these tissues a substance giving typical chemical reactions of histamine, and physiologically indis-

tinguishable from it. It causes a fall in blood pressure in the cat and a rise of blood pressure in the rabbit (urethane anesthesia), when injected intravenously. It stimulates the isolated uterus of the virgin guinea pig and relaxes the uterus of the rat. Both it and histamine, when injected intravenously into guinea pigs or rabbits, produce respiratory disturbance, cyanosis, tremor, cramps and collapse. The conclusion is therefore drawn that "at least one of the active principles of organ extract is histamine."—L. G. K.

(ENDOCRINE) Three cases of abnormal growth (Drei Wachstumsstörungen). Kundraditz, Wien. klin. Wchnschr., 1922, **35**, 663.

The author first reports a case of infantile gigantism with symptoms of acromegaly. The case of a girl of 13 with myxedematous symptoms is also reported. She was about 30 cm. shorter than normal. The skin was dry, with pseudolipomas in the fossae supraclavicularis. The **thyroid** was not palpable. Her intelligence was comparatively good. Injection of 1 mg. of **adrenalin** was not followed by glycosuria and produced even a fall of the blood sugar. The case was diagnosed as congenital hypoplasia of the thyroid. Thyroid extract brought about improvement. A boy of 8 years is described. He was shorter than normal and looked like a cretin. There were only some very slight symptoms of rickets. The skin was dry. Radiography showed normal ossification. The thyroid was not palpable, the very small scrotum was empty, and the child was mentally deficient. This case was diagnosed as pluriglandular insufficiency with special dysfunction of the **hypophysis.** That hypopituitarism was present was proved, according to the author, by the hypoplasia of the gonads, the glycosuria that was sometimes found and the adiposity of eunuchoid type.—J. K.

ENDOCRINE adiposity. Loewy (A.) & Zondek (H.), Ztschr. f. klin. Med. (Berl.), 1922, **95**, 282-292.

An illustrated report of 7 cases of adiposity. The type as described here is found only in females and is characterized by the excellent results obtained with **thyroidin.** Although the patients became much thinner they did not lose their fat where it was most marked and disagreeable. Basal metabolism determinations were of clinical importance only in that they showed that all cases of pathological adiposity are not caused by disturbed metabolic energy. These cases are somewhat similar to cases of hypodystrophy. In some of these the changes in water metabolism are very important, especially when determined by Volhard's method. Thyroidin always raises the respiratory metabolism.—J. K.

Epilepsia y glándules de SECRECION INTERNA. Malamud (T.), Prensa méd. argentina (Buenos Aires), 1922, **9**, 97.

Endocrine disorders often have a part in epilepsy. Certain troubles are perhaps due to the diencephalon.—B. A. H.

(ENDOCRINE) Osteitis fibrosa. Nagelsbach & Westhnes, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1599.

He showed many "endocrine symptoms," details of which are not given.—J. K.

A short note on a patient who died of general osteitis fibrosa.

(ENDOCRINE) The critical age of man (La edad critica del hombre). Navarro (A.), Prensa méd. argentina (Buenos Aires), 1921, **7**, Nos. 12, 13, 14, 15, 18, 19, 20, 22, pp. 146, 159, 172, 183, 220, 234, 244.

A philosophic and scientific exposition on the present and future life and on old age. The author is inspired especially by the work of Marañon and Steinach. He gives in detail the influence of different endocrine glands on the life of man. Several clinical cases are interpreted to agree with these theories.—B. A. H.

(ENDOCRINE) Morphological studies of the lipoid substances in starved animals (Zur Morphologie der lipoiden Substanzen im Hungerzustande). Okuneff (N.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1922, **71**, 99.

Okuneff studied the distribution of isotropic and anisotropic lipoids in the various organs of 6 rabbits starved from 9 to 17 days, during which time the average loss in body weight was 40%. He observed, as many others have noted in other animals, that the weight of the **suprarenal glands** during hunger was often even doubled. He found that the cholesterol ester content of the suprarenal cortex in starvation was distinctly increased. No noteworthy changes in the cell lipoids were observed in the kidney, **thyroid, parathyroids, pancreas, testes** and **hypophysis.** A very great increase in both isotropic and anisotropic lipoids was found in the **thymus** gland. Whether the deposition of lipoids in these tissues during hunger is primary or secondary to the hunger lipodemia cannot be stated.—D. M.

ENDOCRINE glands and the blood (Les glandes à sécrétion interne et le sang). Perrin (M.) & Hanns (A.), Progrès. méd. (Par.), 1922, **37**, 537-538.

A brief review.—F. S. H.

Parabiosis in research on ENDOCRINE GLANDS [Nuevo método para el estudio experimental de la influencia de las glándulas de secreción interna en el desarrollo del organismo (hiperfunctión; estudio teórica)]. Rubinstein (D.), Semana méd. (Buenos Aires), 1921, **28**, 477.

To find the influence of the **hypophysis** on growth the author first combined two young dogs in parabiosis. Later the hypophysis was extirpated from one of the dogs, which caused hypophyseal hypertrophy in the other. The dogs were then separated. The one with the hypertrophied hypophysis presented symptoms of hyperpituitarism. One experiment was performed.—B. A. H.

El cancer y su origen ENDOCRINO. Stajano (C.), Prensa méd. argentina (Buenos Aires), 1922, **9**, 265.

Cancer is said to be caused by nervous disorder, influenced by endocrine factors.—B. A. H.

ENDOCRINE organs and avitaminosis. Thomas, Klin. Wchnschr. (Berl.), 1922, **1**, 2165.

A short note. The animals were fed a vitamin free diet. After death, hemorrhages, hyperemia and pigmentation with hemosiderin were found in all endocrine organs.—J. K.

Morphological variations of ENDOCRINE origin (Contributo alfo studio delle dismorfie endocrine). Vidoni (G.), Arch. di antrop. crim. [etc.] (Torino), 1921, **41**, 438-457, 545-571; abst., Ber. u. d. ges. Physiol. (Berl.), 1922, **14**, 250.

The variations in appearance and behavior due to disorders of endocrine functions are discussed, and especially the facial angle and its importance from the point of view of criminology and anthropology. The author attempts a classification of skull and face forms (those in **acromegaly, myxedema, cretinism,** geroderma, **exophthalmic goiter, eunuchoidism, mongolism,** the adenoid facies and those of **tetany** and of **Addison's disease**). Endocrine disorders are manifested also in the build of the body (size, proportions, fat distribution, pigmentation, distribution of hair and appearance of the nails). The form of the nose and of the ear may be affected by endocrine factors, as may also the condition of the teeth (the falling out of the teeth in exophthalmic goiter, the delayed development of the teeth in **thymus** insufficiency).. Reference is made to the enamel defects in epilepsy. Sexual anomalies are discussed at some length. A case of pubertas praecox is reported in a 12 year old imbecile in whom hyperfunction of the **testis** with accompanying hydrocele is claimed to have a causative relation. The paper ends with a discussion of the possible relations of the endocrine organs to deformities and degenerations in general.—E. C. A.

(ENDOCRINE) Theoretical and practical importance of the endothelial symptom (Zur Theorie und praktischen Verwendbackeit des Endothelsymptoms). Vogt (E.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1007.

The so-called "retico-endothelial system" consists of the "Kupfer" cells; the reticulum cells in the red pulp of the spleen, the lymph glands, and the bone marrow; and in special parts of the connective tissue of the skin, lungs and serosa. This system is very important, especially in the pathology of the blood. It is considered as the seat of haemoglobin and cholesterol metabolism. This last process is, however, changed in pregnancy. The reticulum cells form the "fibrin ferment" and thus play a very important part in blood clotting. Another function is the maintenance of normal tonus of the walls of the blood vessels. When this tonus is too low, stasis of circulation in the forearm, e. g., by an elastic bandage, is followed by extremely small capillary hemorrhages in the skin ("positive endothelial symptom"). In normal persons this symptom is negative, but during menstruation and pregnancy it is positive. In the menopause also, whether caused by ablation of the ovaries or by x-rays, or whether it is quite natural, a positive endothelial symptom is found. The author concludes that physiological changes in the endocrine organs of women (as during menstruation, pregnancy, etc.) give rise to a positive endothelial symptom. The positive symptom after hysterectomy is explained as being due to the supposed endocrine function of the uterus.—J. K.

(ENDOCRINE) Organotherapy in neuroses and psychoses (Organotherapie bei Neurosen und Psychosen). Wagner-Jauregg, Wien. klin. Wchnschr., 1923, **36**, 1-4.

A general uncritical review.—J. K.

Basal metabolism after ingestion of sugar in ENDOCRINE disturbances (Das Verhalten der Standardumsatzsteigerung nach Zuckerzufuhr bei endrokrinen Störungen). Weisz (R.) & Adler (E.), Klin. Wchnschr. (Berl.), 1922, **1**, 1592-1595.

In normal individuals ingestion of saccharose raises the basal metabolism 9.9% to 12.7%. In a patient with **Graves' disease** this raise was 64.4%. In a case of **myxedema** it was 26.3%, but thyroidin caused diminution to normal.—J. K.

(ENDOCRINE) Experimental studies on the importance of organotherapy (Experimentelle Untersuchungen über den Wert der Organtherapie). Zondek, Klin. Wchnschr. (Berl.), 1922, **1**, 1668.

Decomposed products of endocrine glands showed no specific endocrine action. These specific reactions are obtained only by grafts or by administration of extracts which have not undergone chemical changes.—J. K.

(GONADS) Definition and classification of the sexual characters of the Urodela (Définition et classification des charactères sexuels des Urodèles). Aron (M.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 246-247.

Formation and action of TESTICULAR harmozone in the Urodela (Conditions de formation et d'action de l'harmozone testiculaire chez les Urodèles). Aron (M.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 248-250.

The intensity of the manifestations of rut in the Urodela depends on the quantity of harmozone thrown into the organism and the continuity of its action. Secondary sexual characters are unequally susceptible to the action of testicular harmozone.—T. C. B.

(GONADS) The OVARY in different psychoses (Contribution à l'étude de la glande ovarienne dans les différentes psychoses). Ballif (C.), Bull. et mém. Soc. de neurol., psychiat. et psychol. de Jassy, 1921, **3**, 20-22 (September).

The ovaries of 31 psychotic individuals were studied histologically. The greatest amount of lipoids was found in 2 cases of **myxedema.** The distribution extended not only through the **corpora lutea** but also into the primary follicles and the ovisacs. Similar distribution was found in a case of anxious melancholia with a **goiter.** The amount of lipoids was very much diminished in cases of dementia precox, senile dementia, in some cases of pellagra and a case of non-goitrous melancholia. Where confusional states existed, in mania or epilepsy, a normal picture was observed.

—F. S. H.

(GONADS) A case of pseudohermaphroditismus masculinus. Benda, Klin. Wchnschr. (Berl.), 1922, **1**, 2499.

(GONADS) The TESTES in general diseases with particular reference to the changes in the interstitial cells [Die Hoden bei Allgemeinerkrankungen (mit besonderer Berucksichtigung des Verhaltens der Zwischenzellen)]. Berberich (J.) & Jaffe (R.), Frankfurt. Ztschr. f. Path. (Weisb.), 1922, **27**, 395.

A study was made of the testes of one hundred subjects divided as follows: 21 dying of acute illness, 17 to 56 years of age; 50 dying of chronic diseases, 17 to 56 years of age; 6 dying of acute illness, 56 years of age and over; 20 dying of chronic diseases, 56 years of age and over; 2 cases of undescended testis; 1 case of unilateral castration coming to autopsy one year after operation; and 9 cases of fibrosis testis—also included under acute and chronic diseases. The authors used frozen sections stained with fat stains and paraffine sections stained with hematoxylen and eosin. Some of the important observations follow. In young individuals dead of acute diseases there rarely was any injury to spermatogenesis, while the interstitial cells were generally more or less increased. In old men dying of acute diseases, spermatogenesis was usually considerably impaired, and usually very few interstitial cells were present. In chronic diseases in young individuals, no constant changes were found.

About one half of the cases showed impairment of spermatogenesis. The interstitial cells were numerous in those dying of cachexia. In old individuals injury to spermatogenesis was generally a constant finding, but the interstitial cells were rarely significantly increased. The authors could not show any definite relation between the definite diseases and changes in testes. Concerning the "Fettrandzone" of the Sertoli cells, and the lipoid content of the interstitial cells, the authors observed that when the interstitial cells were rich in lipoid, the Sertoli cells were poor, and vice versa.—H. L. J. (D. M.)

(GONADS) The existence of an ovarian gland homologous to the interstitial gland of the testis (Sur l'existence d'une glande ovarienne homologue de la glande interstitielle testiculaire). Berger (L.), Compt. rend. Acad. d. sc. (Par.), 1922, **175** (September); abst., Presse méd. (Par.), 1922, **30**, 967.

The paraganglia of the ovarian hilum are homologous with the accumulation of localized cells in the sympathetic nerves of the testicular hilum, the albuginea, or their vicinity. The paranervous accumulation of the testicle is connected with the interstitial elements and their process of development is the same. While the large paraganglion masses in the testicle make investigation difficult, their scarcity in the ovary permits easier study. The author concludes that since there are paraganglionic elements in the ovary, it is probable that the interstitial gland of the testicle is also to be considered as a paraganglion.—R. G. H.

(GONADS) The action of the internal secretion of the TESTIS and PROSTATE upon metabolism. Bogoslovsky (G. N.) & Korenchevsky (V. G.), Russ. J. Physiol., 1921, **3**, 48-54.

The nitrogen and the gas metabolism were studied in normal and castrated dogs before and after injections of fresh emulsions of the testicles and of the prostate. Both had a much more marked effect on castrated animals. Both emulsions cause an increase in the N metabolism, which may rise in castrated animals, in some cases by 18.9% above that before castration. No definite changes in the gas metabolism were observed. The diuresis is decreased in castrates treated with the testicular emulsion, but in thyriodectomized castrates it is generally increased. Prostate emulsions increase the diuresis; this is more marked in castrates. The general conclusion is that the testicle and the prostate are synergetic glands of internal secretion.—Physiol. Abst., **7**, 449.

(GONADS) Hydrocephalus with obesity (Hydrocéphalie avec obésité). Bonnet, Babanneix & Carrette. Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1723-1731.

A case of probable ovarian insufficiency in which adiposogenitalis was due to congenital syphilis.—F. S. H.

(GONADS) CORPUS LUTEUM extract in hyperemesis gravidarum (L'extrait de corps jaune contre les vomissements de la grossesse). Cheinisse. Presse méd. (Par.), 1921, **29**, 306 (April).

The author points out that it is about fifteen years since M. G. Stella proposed the treatment of pernicious vomiting of pregnancy with ovarian extract. He says that in the last few years ovarian therapy has been taken up in the United States and France by more precise methods, namely, the injection of extract of corpus luteum. The intramuscular and intravenous use of the extract has given favorable results. It is usually productive of no harm but should not be used in goitrous women.—Am. J. Obst. & Gynec., **4**, 450.

(GONADS) A case of true lateral HERMAPHRODITISM in a pig with functional OVARY. Corner (G. W.), J. Urol., 1921, **5**, 481-485.

The specimen described was found among several brought from a slaughter house, so the nature of the external genitalia could not be determined. The specimen itself showed a normal uterus. The left tube and ovary were normal and functional. Corpora lutea were found in the latter and a recently discharged ovum was found in the tube. Sections showed normal ovarian tissue without any trace of testicular tissue. On the right side, the uterine horn ended in a slender tube which became very small and disappeared in connective tissue near the epididymus. At the site of the ovary on this side was a testis, normal in appearance and size. Sections showed normal tubular and interstitial tissue but no spermatozoa. The epididymus, which was normal in appearance, was continued down parallel with the horn of the uterus as the Wolffian duct. This is the first case of true hermaphroditism in swine in which there is absolute proof of the functioning of one of the gonads.—J. C. D.

(GONADS) Experiments on genital hormones (Essai d'expérimentation sur les hormones génitales). Cotte (J.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 842-844.

An attempt to prove the presence of genital hormones on the hypothesis of antigen-antibody. If there is a conflict between hormones, which prevent, for example, the development of a testicle grafted into a female, and if the hormones are colloidal, there may be a production of antibodies under the influence of hormones of the graft. The grafted female would be in some ways anti-male, and might give birth only to females. Female guinea pigs were grafted with a testicle and allowed to breed. The reverse operation was also performed. No positive results were obtained. The female gave birth to both male and females.—T. C. B.

(GONADS) Determination of secondary sexual characters in fish (Etude du determinisme des caractères sexuels secondaires chez les poissons). Courrier (R.), Arch. d'anat., d'histol. et d'embryol. (Strassb.), 1922, **1**, 119-144.

The fresh water fish, Gasterosteus aculeatus, was selected, as it shows in the male well marked secondary sexual characters (color, etc.). These characters are not correlated with the seminiferous tubules, but with the interstitial tissue, which appears at seasons corresponding with those at which the sexual secondary characters are apparent, and only then. This tissue is considered to originate from leucocytes which undergo special differentiation when they migrate into the testis.—Physiol. Abst., **7**, 449.

(GONADS) Uterine hemorrhage of endocrinopathic origin. Geist (S. H.), Surg., Gynec. & Obst. (Chicago), 1922, **34**, 790-793 (June).

The author believes that all cases of uterine hemorrhage, not associated with tumors that are ulcerated, necrotic or friable, or with conditions that may be dependent on purely local pressure or congestive phenomena such as tubal pregnancies, inflammatory diseases or displacements, and accompanied by a definite pathological—almost pathognomonic—condition of the mucosa, are dependent on some disturbance of ovarian function, with probably disorder of other endocrine glands as well. This endocrine disorder expresses itself in a "hypertrophy of the mucosa," which tissue may be the source of some chemical stimulus that initiates and maintains the bleeding. All these cases can be cured by removal of the ovaries or by x-raying in proper doses.—E. N.

(GONADS) TESTICLES after ligation. Gohrbandt (E.), Arch. f. klin. Chir. (Berl.), 1922, **120**, 637-647 (September).

Gohrbandt omitted the ductus deferens and the deferential artery from the ligation, in his experiments on rabbits, but the testicles became partially or entirely atrophied and function seemed totally lost even in the islands of apparently normal tissue.
—J. Am. M. Ass., **79**, 1887.

(GONADS) X-rays and reproduction in rats. Hooker (D. R.), Am. J. Hyg. (Balt.), 1922, **2**, 461-462.

The effect with moderate and large doses is sterilization. Small doses stimulate. There is no effect on the interstitial tissue, nor on weight and growth.—Physiol. Abst., **7**, 450.

(GONADS) The interstitial cells of the urodele TESTIS. Humphrey (R. R.), Am. J. Anat. (Phila.), 1921, **29**, 213-278.

The testes of urodeles are found to be very favorable material for the determination of interstitial cell correlations. Humphrey

shows that the development of the interstitial cells in urodeles is correlated with the regressive phases of the spermatogenic cycle. The urodele interstitial cell is but a temporary modification of a stromal cell. No evidence has been found that the interstitial cells constitute a gland of internal secretion. Secretion products other than lipoid substances have not been observed. The value of the interstitial cells to the organism during their period of hypertrophy remains problematical.—W. J. A.

(GONADS) The histology of TESTIS from a case of human hermaphroditism, with a consideration of the significance of hermaphroditism in relation to the question of sex differentiation. Jordan (H. E.), Am. J. Anat. (Phila.), 1922, **31**, 27-53.

The testis described was removed from the right groin of a woman 45 years of age. A sister and a niece of the woman both showed a similar type of hermaphroditism. Histologically, remnants of seminal tubules and masses of interstitial cells predominated. Jordan has added a very interesting discussion of hermaphroditism and of sex differentiation in general.—W. J. A.

(GONADS) The action of radium emanation on the uterus and OVARIES of guinea pigs (De l'action de l'emanation du radium sur l'uterus et les ovaires des cobayes). Katzareff (A.) & Mollow (M.), Gynéc. et Obst. (Paris), 1922, **6**, 244-276.

The application of radium emanation to one horn of the uterus of guinea pigs produced symptoms of shock in a few hours. Hyperemia, edema and necrosis of the uterine tissue was found, accompanied by exudates into the uterine cavity, rich in polynuclears and particularly eosinophils. Infiltration of eosinophils into the tissues also occurred. The muscular fibers, endothelial and glandular cells showed vacuolar degeneration which was either granular or hyaline. The nuclei were vesicular. In the ovary hyaline degeneration, granular or vacuolar, was found. The germinal epithelium was degenerated. The vessels were engorged with blood. Smaller doses produced lesser effects, but of the same type. The ovaries often became cystic.—F. S. H.

(GONADS) Lipoids in the INTERSTITIAL CELLS (Uber den Lipoidstoffwechsel der männlichen Keimdrüsen). Kleinicke (K.), Frankfurt. Ztschr. f. Path. (Weisb.), 1922, **27**, 185-196.

In the interstitial cells of degenerated testes the amount of phosphatides in comparison to the other lipoids is reduced. Cholesterol esters are often found in these cells in degenerated testes. The increased quantity of other lipoids is believed to be due to absorption from the spermatic epithelium.—Physiol. Abst., **7**, 449.

(GONADS) The effect of combinations of substances which act on the uterus (Ueber die Wirkung von Kombinationen der Uterusmittel). Kosakaé (J.), Ztschr. f. Geburtsch. u. Gynäk. (Stuttg.), 1922, **85**, 364-395.

Protein and cholin-free extract of **placenta** induces uterine contractions similar to other extracts, but not particularly strongly in the early stages. The tonus of the uterus tends to decrease after the first effect has passed off. A second injection increases the tonus. Rhythmical uterine contractions similar to those occurring during parturition appear after the injection of placenta extract. This effect is more marked if **hypophysis** extract is combined with the placental. The reaction is intensified by repeated doses. The injection of **adrenin** in rabbits and guinea pigs does not initiate uterine contractions but seems to favor those already occurring. This effect is intensified when the 3 extracts are given together.—F. S. H.

(GONADS) MENSTRUATION and the nervous system (Menstruation et système nerveux. Essai sur les problemes physiologiques et pathologiques). Kreis (J.), Bull. Soc. d'obst. et de gynéc. de Par., 1922, **11**, 610-624.

A review.—F. S. H.

(GONADS) TESTICLE implants (Hodentransplantation). Kreuter, Deutsche Ztschr. f. Chir. (Leipz.), 1922, **172**, 437 (July).

Kreuter remarks that microscopic examination later of a transplanted testicle is the only way to determine the actual facts in regard to gonad grafts, instead of merely subjective impressions. He knows of only one report of this kind (Rössle), but has had opportunity himself in two cases to remove an implanted testicle three weeks and two years after the grafting operation. Complete necrosis of the reproductive elements and extreme reduction of the interstitial cells was found in the testicle removed in three weeks. In the other case, the ingrafted testicle had been totally absorbed in the course of the two years. His experience teaches that grafting an undescended testicle from a heterosexual subject in a homosexual subject who has had one testicle removed has no effect on the homosexual impulses. In another experience, a homosexual testicle implanted after total castration in a sexually normal individual did not display any influence on the sexual impulses.

—J. Am. M. Ass., **79**, 1463-1464.

(GONADS) The so-called compensatory hypertrophy of the TESTICLE after unilateral castration. Lipschütz (A.), J. Physiol. (Lond.), 1922, **56**, 457-458.

Experimental evidence justifying the opinion that the hypertrophy after unilateral castration is only apparent, the development being more rapid after the removal of one testicle, and never

exceeding in final weight that of a normal testicle. Not only is there no hypertrophy of endocrine tissue, but there is no hypertrophy at all.—T. C. B.

(GONADS) A case of eunuchoid gigantism (Ein Geval van eunuchoiden reuzengroei). van Luyt (C.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, **66** (II), 1748-1752.

Report of a case of a man of 20 years, 1.81 M. in height and 67 kg. in weight. He had a boyish voice, very small sexual organs, no beard and no hair in the axillae or on the pubes. Sexual desires did not exist, though the man sometimes had erections without ejaculations. A radiogram of the skull showed nothing noteworthy. Carbohydrate tolerance was high.—J. K.

(GONADS) The hypogenital hand, or acrocyanosis. Marañón (G.), Siglo méd. (Madrid), 1921, **68**, 672-675 (July 16).

Marañón is convinced that the vasomotor disturbances inducing the acrocyanosis are traceable to insufficiency of the genital glands, predominantly of the ovaries, and hence his term "hypogenital hand." There may be insufficiency of other endocrine glands, but the genital insufficiency is predominant and constant. A glimpse of the congested cyanotic, clammy hands is enough to suggest genital infantilism; the hands are usually puffy and doughy, and the nails are often spotted. The age is between puberty and maturity or at the menopause, and the subjects are usually females. Time and organotherapy are the reliance in treatment, especially intensive and prolonged ovarian treatment. Heliotherapy has also yielded excellent results in his hands, both for acrocyanosis alone or associated with tuberculosis or other chronic infection.—J. Am. M. Ass., **77**, 1057.

(GONADS) Fibroma and sarcoma of the OVARY; report of two unusual ovarian tumors. Meigs (J. V.), Boston M. & S. J., 1922, **187**, 952-956.

Two illustrated case histories, and an account of the pathological findings. These are not of direct endocrine interest.—J. C. D.

(GONADS) The origin of the so-called luteal cells in the TESTIS of hen-feathered cocks. Nonidez (J. F.), Am. J. Anat, (Phila.), 1922, **31**, 109-124.

The so-called luteal cells, which were supposed by Boring and Morgan to account for the hen-feathering of Sebright bantam cocks, are found by Nonidez to arise during degeneration of the sexual cords and early seminiferous tubules. This occurs as the result of fatty infiltration of certain elements of the seminal epithelium. The spermatogonia and many of the columnar epithelial cells disappear without leaving any trace of their former existence. Remnants of

the sexual cords in the form of clusters of luteal cells were also found in the testes of young birds of breeds other than the Sebright.
—W. J. A.

(GONADS) The origin and histogenesis of epithelioma of the adult TESTICLE in man (Sur l'orgine et l'histogénèse de l'épithélioma séminifère du testicule adulte chez l'homme). Peyron (A.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 842.

A demonstration, the communication to be published later.
—T. C. B.

(GONADS) The "all or none" law and gynandromorphism in birds (La loi du "tout ou rien" et le gynandromorphisme chez les oiseaux). Pézard (A.), J. de Physiol. et de path. gén. (Par.), 1922, **20**, 200-211.

Various operations (total or unilateral castration, or castration followed by implantation of minute fragments of **testicle**) were performed on young Leghorn cocks at the time when secondary characteristics began to appear. At autopsy after full development widely different amounts of testicular tissue were present. Nevertheless, in the series of animals there were only two types, as judged by growth of the comb, the wholly sexed and the wholly neutral, without intermediate forms. The rate of growth of the comb was independent of the amount of active testicular tissue; and its decrease in size after castration was not affected by the presence of small testicular nodules. If the nodules became effective in inducing a renewed growth of the comb, the normal curve of resumed growth started at once and without transition from the period of regression. The "all or none" law, therefore, applies to the male characters, but the minimal effective amount of testicular tissue may not be the same for all. The secondary sex characters of the hen seem to obey the same law.—W. B. C.

(GONADS) Dercum's disease and OVARIAN opotherapy (Contributo allo studio della malattia di Dercum e opoterapia ovarica). di Poggio (E.), Rassegna di clin., terap. [etc.] (Roma), 1922, **21**, 129-135.

The author has obtained good results in the treatment of a case of Dercum's disease with ovarian extract.—G. C.

(GONADS) Pseudohermaphroditismus masculinus internus with transverse displacement of the TESTIS (Zur Kenntnis des Pseudohermaphroditismus masculinus internus mit "Dystropia transverse testis"). Priesel (A.), Frankfurt. Ztschr. f. Path. (Weisb.), 1921, **26**, 80.

The case is reported of a man, aged 77 years, who died of symptoms of scurvy. At autopsy in an otherwise normal individual

there was found a persistence of the Mullerian ducts which had become differentiated into Fallopian tubes, uterus and vagina.
—H. L. J. (D. M.)

(GONADS) Function of the interstitial cells of the TESTICLE (Die Funktion der zwischenzellen des Hodens). Raffé (R.), Klin. Wchnschr. (Berl.), 1922, **1**, 1482.

When spermatogenesis is disturbed the interstitial cells may be increased or decreased in number. The interstitial cells have a trophic as well as an endocrine function, but of these functions nothing is known with certainty.—J. K.

(GONADS) Steinach operation for dementia praecox (Contribución al estudio dela demencia precoz. El tratamiento de la demencia precoz por el metodo de Steinach para las tituladas curas de rejuvenimiento). Raitzin (A.), Semana méd. (Buenos Aires), 1922, **29**, 1238.

In two cases of catatonic dementia praecox the Steinach operation was performed. The mental condition was not improved. One of the patients died, 7 months after the operation, of tuberculosis.
—B. A. H.

(GONADS) Modifications determined by x-rays in the rabbit's OVARY (A propos des modifications déterminées par les rayons X dans l'ovaire de la lapine). Regaud (C.) & Lacassagne (A.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 938-940.

A reply to Salazar (Compt. rend. Soc. de biol., 1922, **87**, 703).
—T. C. B.

(GONADS) Homosexualiteit. Rogge (H. C.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1922, **66** (II), 1068-1075.

General article.—J. K.

(GONADS) TESTICLE transplantation (Ueber die neueren Bestrebungen der Hodenverpflanzung). Rosenthal (O.), Med. Klin. (Berl.), 1922, **18**, 370-371.

Criticism of the custom of unilateral transplantation of testes. The author believes that the operation may eventually cause a concealed malady or a trauma in the man from whom the testis is taken. The likelihood of immoral commerce in testicles is given as another argument against this practice.—A. B.

Irradiation of the OVARY of the rabbit: the law of radiosensibility of Bergonié and Tribondeau (A propos de l'irradiation de l'ovaire de la lapine: quelques doutes au sujet de la loi de radio-sensibilité de Bergonié et Tribondeau). Salazar (A. L.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 703-705.

Histological and critical.—T. C. B.

(GONADS) Sex glands of mammals. II. Resection of the vas deferens (Etudes experimentales sur les glandes sexuelles chez les mammifères. II. Experiences sur la résection du "vas deferens"). Sand (K.), J. de Physiol. et de path. gén. (Par.), 1921, **19**, 494-503.

Resection of the vas deferens before puberty is without influence, and thereafter it affects testicular structure only slowly; six months or a year may be required before effects are seen. Transection is equivalent to resection. Unilateral resection with contralateral castration results in extreme tubular atrophy and extraordinary hypertrophy of the Leydig cells, which favors the theory that they are the source of male sex hormones. Sex characters developed normally in all cases and sex activity was marked, though there was almost total tubular atrophy. The animals used were rabbits, guinea pigs and rats.—W. B. C.

(GONADS) Röntgen ray castration in man (Ein Beitrag zur Röntgen-Kastration beim Mann). Schinz (H. R.), Schweiz. med. Wchnschr. (Basel), 1922, **52**, 886-889.

A review of the application of Röntgen rays to castration of man. Four cases from the literature and one case observed by the author are cited. The relative dosage for temporary and total castration for men and women is given.—A. T. R.

(GONADS) Steinach Operationen. Schreiber (F.), Beitr. z. klin. chir. (Tübing.), 1922, **127**, 212-213.

Report of 4 cases. One was a very senile man of 65 with arteriosclerosis and polyneuritis. The only effect of the operation was three erections after ligation of the vas deferens. A man of 67 had arteriosclerosis and apoplexy. He had one erection after the Steinach operation, but no other improvement. The third case was a very senile man with trigeminal neuralgia. There was no improvement after the operation. A homosexual patient was castrated and a cryptorchic testicle, which was completely changed into connective tissue, was transplanted from a boy of 16. After a period during which he showed only pederastic symptoms he said he felt some heterosexual inclination but remained impotent.—J. K.

(GONADS) Pubertas praecox in epidemic encephalitis (Ueber Pubertas praecox bei epidemischer Encephalitis). Stern (F.), Med. Klin. (Berl.), 1922, **18**, 842-845.

Report of a boy, 13½ years old, who 2 years before had had grippe, followed by somnolence and later by some amyostatic symptoms, especially in the musculature of the head, neck and left arm. No sign of pituitary trouble was apparent. One and a half years later there was a sudden deepening of the voice and soon consider-

able growth of the **gonads** (penis 11 cm. long, **testes** like walnuts), abundant growth of hair on the trunk and pubic region and development of a mustache. Masturbation and pollutions occurred. Spermatozoa were found. In the previously intelligent child psychical changes set in. He became restless and incompatible. There was no psychic prematurity sexually. Considerable increase of lymphatic and eosinophile cells was noted in the blood. No tumor of testis or **adrenal** cortex could be determined. The author concludes, according to the well-known theories of a connection between hypopinealism and pubertas praecox (especially in hypoplasia of the **pineal**, Askanazy and Brack), that there was direct damage of the pineal through the inflammatory products of encephalitis, thus causing hypofunction and sexual prematurity.—A. B.

(GONADS) Organotherapy in OVARIAN hemorrhage (Klinische untersuchungen über den Wert der Organotherapie bei ovariellen Blutungen). Stickel (M.) & Zondek (B.), Ztschr. f. Geburtsch. u. Gynäk. (Stuttg.), 1922, **85**, 83-106.

Unsatisfactory and contradictory results were obtained.
—F. S. H.

(GONADS) Sex and age (Geschlecht und Lebensalter). Straatz, Klin. Wchnschr. (Berl.), 1922, **1**, 1668.

The influence of the secondary sexual characteristics on the body are due only in a small degree to endocrine influences. The authors believe that these characteristics are influenced most of all by heredity.—J. K.

(GONADS) On a case of eunuchoidism. Sumiwo (S.), Chyugwai Iji-Shimpo, 1922, **42**, No. 1011; No. 1012 (May); cit., Jap. Med. World, **2**, 303.

(GONADS) Corpus luteum and ovariotomy during pregnancy. Szymanowicz (J.), Polska Gaz. Lekarska (Lemberg), 1922, **1**, 554 (July); cit. J. Am. M. Ass., **79**, 1808.

(GONADS) Genital infantilism. Wohlauer, Klin. Wchnschr. (Berl.), 1922, **1**, 1626.

A man of 18 with well developed crines pubes, undescended testicles, important changes in teeth and skull (no more details as to the changes are given) and symptoms of tetany (positive Chvostek and Erb symptoms). The relation of latent tetany and hypofunction of the gonads is probable, as is shown by the studies of Melchior.
—J. K.

(GONADS) Steinach operation (Wann und wie ich ohne Erfolg gesteinacht wurde). Zeissl (M.), Wien. klin. Wchnschr., 1922, **35**, 764-765.

The author suffered from hypertrophy of the prostate. Vasectomy on both sides had no effect. The rejuvenation which, according to Steinach, should follow this operation was not seen. The author considers the Steinach operation useless.—J. K.

(GONADS) The effect of x-rays on the internal secretion of the OVARY (Experimentelle Untersuchungen über die Beeinflussung der inneren Sekretion des Ovariums durch Röntgenstrahlen). Tsukahara (I.), Ztschr. f. Geburtsch. u. Gynäk. (Stutt.), 1922, **85**, 36-48.

When both ovaries are removed from rabbits a hypersensitiveness to **adrenin** is found, as is shown by a hyperglycemia which lasts for some hours after doses of usual ineffectiveness. This sensitivity is at a maximum 2 months after castration. A bilateral administration of the castration x-ray dose on the ovaries brings about the same sensitivity. The follicular apparatus is damaged, the ripening follicle being harmed the most. The castration dose produces no changes in the uterus. The eosinophil cells of the **hypophysis** are greatly increased.—F. S. H.

(GONADS) Present status of knowledge of MENSTRUATION (Der heutige Stand der Lehre von der Menstruation). Seitz (A.), Med. Klin. (Berl.), 1922, **18**, 1013-1017 (August).

A short review of the newer knowledge of menstruation, especially from the standpoint of the histological cycles in the endometrium and the ovary.—E. N.

Sclérodermie et HYPOPHYSE. Bénard (R.) & Coulaud (E.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1518-1524.

Brief bibliographic review.—F. S. H.

ADIPOSO HYPOPHYSEAL syndrome following epidemic encephalitis (Sindrome adiposo-ipofisaria consecutiva ad encefalite epidemica). Bertolani (A.), Riv. di patol. nerv. (Firenze), 1922, **27**, 72-74.

Report of the cases of two women with adiposo hypophyseal syndrome following epidemic encephalitis. It might have been a question of an inflammatory atrophy of the hypophysis after infection, as reported by Massalongo and Piazza, or it might have been due to inflammatory lesion of the gray substance of the infundibulum and that below the floor of the third ventricle. The author believes in what he calls a mixed theory, that a primitive lesion of either may have interrupted the interrelation between the pituitary and some nervous centers.—G. V.

(HYPOPHYSIS, GONADS). A pluriglandular syndrome following influenza (Su un cas di sindrome pluriglandolare consecutive ad influenza). Bosisio (R.), Folia med. (Napoli), 1922, **8**, 394-400.

Report of a girl who, after influenza, presented various symptoms which led to a diagnosis of hypophyseal and gonadal insufficiency.—G. C.

HYPOPHYSEAL dwarfism (Nanismo hipofisaria de Aschner-Paltauf). Castex (M. R.) & Waldorp (C. P.), Rev. Asoc. méd. argent. (Buenos Aires), 1921, **34**, 47-68; Semana méd. (Buenos Aires), **28**, 564.

A report of two cases. The subjects were dwarfs, with well developed genital organs, the intelligence of adults, and small sella turcicas. In one case there was anterior hypopituitarism, plus polyuria. The two patients were heredosyphilitic.—B. A. H.

The secretory cycle of the cells of the HYPOPHYSIS (Sur le cycle sécrétoire de la cellule hypophysaire). Collin (R.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 549-551.

Histological.—T. C. B.

Extracts of HYPOPHYSIS and blood coagulation (Etude sur l'action des extraits d'hypophyse sur la coagulation sanguine). Feissly (R.), Presse méd. (Par.), 1922, **30**, 997-998.

Feissly investigated whether the increased coagulation of the blood following the use of extracts of the posterior lobe of the hypophysis was to be attributed to some specific substance contained in the gland, or to substances occurring also in extracts of other tissues. Extracts were made from various organs either by simple maceration without heating, or by maceration followed by heating in an acid medium. Experiments with these extracts as well as with pituglandol, pituitrin, luteoglandol, splenoglandol and even with the antuitrine of Parke Davis (an extract made of the anterior lobe of the hypophysis) produced acceleration of the blood coagulation in vivo. The changes in coagulability were determined with the very delicate instrument devised by Feissly. The results were checked by Fonio's method, which is based on an entirely different procedure. The extracts obtained by simple maceration were found to possess strongly thromboplastic properties both in vitro and in vivo; the boiled extracts, on the other hand, gave no evidence of thromboplastic activity in vitro, yet they increased coagulability in vivo, showing that coagulation must be connected with some kind of reaction within the organism. No increase of prothrombin or decrease of anti-thrombine could be demonstrated, but a definite and powerful enzyme action was observed. The effect of extracts on man were studied, special attention being given to the duration of increased coagulability and the occurrence of a phase of decreased coagulability. Blood samples were taken at intervals of 13 minutes, 1 hour and 7 hours after injection of the extracts. A certain degree of increased coagulation was found, which occurred also in

vitro and was more marked in plain glass tubes than in paraffin-coated ones; but very definite decrease of coagulation followed; both phenomena seemed entirely independent of the blood pressure which always rose one-half hour after injection. Feissly warns against the indiscriminate use of such extracts and calls attention to the fact that peptones are known to produce a very distinct anti-thrombine reaction in dogs and none in rabbits. Non-boiled extracts tend to increase the blood pressure; boiled extracts lower them unmistakably. In the main the boiled extracts act like very weak solutions of peptones; the changes in the blood pressure can be obviated by giving them subcutaneously, whereas intravenous injection produces severe reactions; a second subcutaneous injection, given 2 hours after the first, again produces well-marked increase in the coagulability of the blood. While all of these extracts are physiologically active—and powerfully so—there is no evidence that the increase of blood coagulability can be ascribed to pituitary extracts alone.—G. L.

(HYPOPHYSIS) The control of pituitary lesions, as affecting vision, by the combined surgical, x-ray, radium treatment. Frazier (C. H.), Arch. Ophth. (New Rochelle, N. Y.), 1921, **50**, 217-226.

The first part of the paper is taken up with a consideration of the operative methods, their disadvantages and unsatisfactory results. The author emphasizes the frequency with which the early eye defects in hypophyseal cases are overlooked. Four cases are reported in which the use of radium and x-ray following operation prevented or delayed the return of the symptoms. Three of these were subsellar decompressions. One case has a history covering 4 years since operation. The author points out that more evidence is needed. He recommends subsellar decompression followed by x-ray and radium. The removal of the floor of the sella enables these agents to act more directly on the tumor.—J. C. D.

(HYPOPHYSIS) Nervous syphilis and symmetrical cervical lipomatosis (Sifilide nervosa e lipomatosi cervicale simmetrica). Frigerio (A.), Riv. di patol. nerv. (Firenze), 1922, **27**, 513-522.

The author reports a case of neuro-syphilis in which dystrophia adiposa developed immediately after the nervous and mental symptoms. On account of decreased sexual power, somnolence, feeling of cold and asthenia the author believes that the syphilitic infection which caused the nervous symptoms may have produced a lesion of either the hypophysis or the hypothalamic region.—G. V.

HYPOPHYSEAL cachexia (Beitrag zum Bilde der hypophysären Kachexie). Knoll (W.), Wien. Arch. f. inn. Med., 1922, **4**, 555-572.

Hypophyseal cachexia, in Germany also called "Simmonds' disease," is rather rare. In this article a case is described and the literature is reviewed. The author concludes that it is a well defined disease. The cardinal symptoms are precocious senility, loss of body hair, loss of sexual functions, and dullness. The symptoms generally develop long after the lesion (embolus of an arteriola propria of the hypophysis) which caused the disease takes place. Cases have been reported in which this embolus was caused by tuberculosis, syphilitic or septic infections, the last class containing cases of puerperal fever almost entirely. This probably explains why the disease is much more frequent in women than in men. It is highly probable, though the reported cases are not yet absolutely convincing, that pneumonic infections may also give rise to Simmonds' disease. The disease is seen only in adults. For diagnosis the Abderhalden test with an antigen from the pars anterior of the pituitary is recommended by the author. "Forme fruste" of Simmonds' disease is amenable to treatment, though diagnosis may be extremely difficult, especially when other diseases complicate the clinical picture. Tuberculosis of the hypophysis is suggested as another cause of the disease. The author thinks that this disorder may often pass unnoticed, hence may not be so rare as is generally believed.—J. K.

So-called HYPOPHYSEAL infantilism with tumor of the third ventricle and intact HYPOPHYSIS (Infantilisme dit hypophysaire par tumeur du troiséme ventricule. Intégrité de l'hypophyse). Lereboullet (P.), Mouzon (J.) & Cathala (J.), Rev. neurol. (Par.), 1921, **28**, 154-159.

Report of the case of a young man who stopped growing at 13 years of age; at 17 years he presented true signs of intracranial tumor, with hemianopsia among other ocular disturbances; at 23 years he had the appearance of a boy of 14 with scarcely perceptible obesity and complete genital atrophy. Four years later he was fatter and seemed to show a Babinski-Frölich's adiposogenital syndrome. He grew 7 centimeters during this period. He became completely blind in one eye and had hemianopsia in the other. The sella turcica was normal, but calcifications of the clinoidal region suggested the presence of a neoplasm. The patient died 13 years after the beginning of his troubles and at autopsy the case seemed relatively typical. A tumor was found, projecting in the interpeduncular space of the brain, limited by a calcareous layer on the chiasm and compressing the pituitary stalk. The tumor occupied the entire middle region from the inferior wall of the lateral uninjured ventricles to the base of the brain. This tumor was histologically a papillary epithelium of the third ventricle. The hypophysis, more flattened than normal, weighed 44 centigrams, but presented no histological lesion; the other endocrine glands were normal. This case may be compared with those of Vigouroux and Delmos, and

of Marañon and Pintos, thus throwing light upon the problem of the respective rôles of the hypophysis and of the floor of the third ventricle in the genesis of adiposogenitalis. Although the hypophysis was intact, the infundibular stalk was compressed by the tumor. The authors discuss the two possible interpretations, hypophyseal and tubero-infundibular, but come to no formal conclusion.

—Author's Abst.

DIABETES INSIPIDUS of HYPOPHYSEAL origin (Manifestacione soculares en un enfermo con diabetes insipida de origen hipofisario). Marin (A.), Arch. de oftal. (Barcelona), 1921, 250; 533-542.

Owing to its anatomical situation, when there is enlargement of the hypophysis, the optic chiasma is compressed in such a way that completely distinct affections such as **acromegaly** and Frölich's syndrome present identical or similar visual lesions. In the one case the author encountered visual acuteness, dyscromotopsia, papillary atrothy in both eyes and bitemporal hemianopsia. Opotherapy (injections of pituitary) notably improved the acuteness of chromatic vision and slightly the general visual, but the deeper lesions remained in the same condition.—E. B.

(HYPOPHYSIS) On the maintenance of "obstetric anesthesia" by means of infundibulin and chloroform. Martin (A. F.), Brit. M. J. (Lond.), 1922, **ii**, 672-674.

Light chloroform anesthesia commencing with the onset of labor pains, plus repeated small doses of infundibulin, are recommended to maintain an active uterine reflex. When cervical relaxation is practically complete, 0.5 cc. of infundibulin is injected intramuscularly and as the pains increase intermittent chloroform anesthesia is given. After about one-half hour the vigor of the pains abates and the infundibulin is repeated. Six doses in 3 hours is the greatest number cited. The average is 3 doses in 1½ hours. This treatment does not increase the number of postpartem hemorrhages and no toxic effects have been observed, although a few of the patients have shown increased pulse rates toward the end of and after labor. Thirty-two cases were studied.—R. E. K.

HYPOPHYSEAL cachexia, pituitary coma and pituitary lethargy. Mieremet (C. W. G.), Geneesk. Bl. u. Klin. en Lab. v. d. prakt. (Haarlem), 1922, **23**, 235-268.

Complete or incomplete destruction of the anterior lobe of the hypophysis may cause hypophyseal cachexia, as described by Simmonds, but the same anatomical lesion may also cause coma or lethargy. In these cases organotherapy with hypophysis is sometimes effective. The cachexia as well as the coma and pituitary lethargy may have different causes, such as emboli, tuberculosis,

syphilis, malignant or benign tumors and inflammations of unknown origin. The author describes a case which is especially remarkable because the patient was a man, whereas nearly all cases of this kind are in women. He points out that pathologists should observe at autopsy the hypophysis of subjects who die of encephalitic lethargy.
—J. K.

(GONADS) Visual troubles in Frölich's disease (Trastornos visuales en la enfermedad de Fröelich). Poyales, Arch. de oftal. (Barcelona), 1921, 246-302; 307.

Ophthalmoscopy often permits diagnosis in advance of hypophyseal manifestations. The enlargement of the gland determines a series of visual troubles that may be classified in two groups, namely, functional and organic. Among the functional disturbances the most important are bitemporal hemianopsia, augmentation of the blind spot and the existence of scotomata in the stereoscopic vision. Those included in the organic group are optical neuritis, optic hemiatrophia, post neuritica and exophthalmos in both eyes.—E. B.

The influence of x-rays on the HYPOPHYSIS (Experimentelles zur Röentgenbestrahlung der Hypophyse). Rahm (H.), Beitr. z. klin. Chir. (Tübing.), 1922, **126**, 642-657.

When the hypophysis of rabbits is exposed to a stimulating dose of x-rays the rapidity of growth may be increased; in man the same experiment may be followed by temporary diabetes insipidus. Large concentrated doses of x-rays on the hypophysis diminishes or completely arrests growth. It is impossible to decide whether these experiments are important in human pathology.—J. K.

The influence of PITUITARY extracts on the absorption of water from the small intestine. II. Action of pituitary extracts when introduced into the alimentary canal. Rees (M. H.), Am. J. Physiol. (Balt.), 1922, **63**, 146-150.

It has been shown that subcutaneous injections of pituitary extracts delay the absorption of water. In this paper it is shown that the same is true when pituitary extracts are introduced directly into the lumen of the small intestine in dogs and cats.—T. C. B.

The Golgi apparatus in the glandular cells of the HYPOPHYSIS. Functional polarity and the secretory cycle (L'appareil de Golgi dans les cellules glandulaires de l'hypophyse. Polarité fonctionnelle et cycle sécrétoire). Reiss (P.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 255-256.

Combining the Cajal technique with those methods which demonstrate the commoner cytoplasmic and nuclear structures, the author has studied the hypophysis in the calf, dog and cat. Best

results were obtained in the last. An attempt is made to interpret the secretory processes of the hypophysis on the basis of the changing position of the Golgi apparatus in the secretory cells.—W. J. A.

Cachexia of HYPOPHYSEAL origin (Zur Klinik und Therapie der "Kachexie hypophysären Ursprungs"). Reye (E.), Deutsch Ztschr. f. Nervenh. (Leipz.), 1921, **68**, 153-158.

The clinical history of a married woman 50 years of age who has been treated at intervals for several years with pituitary extract (anterior lobe) with good results. Eleven references are given.
—A. T. R.

(HYPOPHYSIS) Essential polyuria or true DIABETES INSIPIDUS (La polyurie essentielle ou diabète insipide vrai). Lortat-Jacob & Turpin, Ann. de méd. (Par.), 1922, **12**, 480-512.

Optic nerve atrophy from vascular pressure due to tumor of the HYPOPHYSIS (Atrophie de Sehnerven durch Gefssdruck bei Hypophysistumor). Siegrist, Arch. f. Ophth. (Berl.), 1921, **105**, 1069-1074.

A case of optic nerve atrophy due to a tumor of the hypophysis (chief cell adenoma, 10-12x22x25 mm. in size) which pressed the optic nerves against the anterior cerebral arteries sufficiently to produce atrophy of nerve fibers.—A. T. R.

(HYPOPHYSIS) The administration of PITUITRIN at the beginning of the third stage of labor. Ryder (G. H.), Am. J. Obst. & Gynec. (St. Louis), 1921, **2**, 61-66 (July).

From a study of 100 cases the author concludes that the administration of pituitrin is a safe procedure at the beginning of the third stage of labor. It tends to cause spontaneous expulsion of the placenta and to lessen the amount of blood lost. It makes guarding of the fundus during the third stage easier and does away with the necessity of watching or holding it. In this series Burroughs Wellcome's preparation of pituitrin was injected hypodermically at the beginning of the third stage. The fundus was then held for twenty minutes, unless the placenta was expelled spontaneously before that time. The author suggests, however, that it is probably better not to wait twenty minutes as a routine before trying to express the placenta. Because of its effectiveness in quickly checking hemorrhage, a hypodermic syringe of pituitrin should be ready for instant use during and after the third stage of every labor.—E. N.

Retardation of metamorphosis in the Colorado axolotl by the intraperitoneal injection of fresh bovine HYPOPHYSEAL anterior lobe substance. Smith (P. E.) & Smith (Irene B.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1922, **20**, 51-52.

This treatment resulted in marked retardation of metamorphosis, which was the reverse of the result expected. There was a decided darkening of the animals.—J. C. D.

Choristoma of the NEUROHYPOPHYSIS with edema (Ein Choristom der Neurohypophyse bei ausgebreiteten Oedemen). Sternberg (C.), Centralbl. f. allg. Path. u. path. Anat. (Jena), 1921, **31**, 585-591.

The author reports a case of a man aged 65 years who, on admission to the hospital, had increased fatigability, marked edema and anemia of about one year's duration. No clinical diagnosis was made. At autopsy extensive medullary carcinoma of the stomach was found. Examination of the pituitary revealed a normal anterior lobe, while the posterior lobe was slightly larger and firmer than average. Microscopic examination showed that in the posterior lobe there was a small mass, less than a millimeter in diameter, made up of very large polygonal cells containing pigment. These cells would under ordinary examination be called ganglion cells, although Sternberg considers them as giant glial cells, described by Stoerck under the name, "monstergliazellen." The author discusses the possibility that these giant glial cells increased the activity of the posterior lobe sufficiently to interfere with salt and water excretion.—H. L. J. (D.M.)

(HYPOPHYSIS) Etiology and pathogenesis of DIABETES INSIPIDUS (Etiologia y patogenia de la diabetes insipida). Udaondo (C. B.) & Carulla (J. E.), Prensa méd. argentina (Buenos Aires), 1922, **9**, 333. **Poliuria cerebral.** Houssay (B. A.), 2d Congr. nacion. de med., Buenos Aires, 1922, September 1-8.

The two reports discuss the pathogenesis of diabetes insipidus and arrive at the conclusion that it is dependent upon the tuber cinereum and not upon the hypophysis.—B. A. H.

(HYPOPHYSIS) DIABETES INSIPIDUS and disorders of character in a case of epidemic encephalitis (Diabéte insipide et troubles du caractère dans un cas d'encephalite épidémique). Urechia (C. I.) & Rusdeá (N.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1492-1497.

HYPOPHYSIS and diencephalon (Hipófisis y diencefalo). Waldorp (C. P.), Prensa méd. argentina (Buenos Aires), 1922, **9**, 309.

This author believes that dystrophia adiposogenitalis and diabetes insipidus are not due to hypophyseal insufficiency, but that they are produced by changes of the diencephalon.—B. A. H.

The erythropoietic function of the HYPOPHYSIS (Recherches expérimentales sur la fonction érythropoïétique de l'hypophyse). Watrin (J.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 907-908.

Histological. Other conditions than gestation give rise to erythropoietic centers in the hypophysis.—T. C. B.

Erythropoietic centers in the HYPOPHYSIS of the pregnant guinea pig (Foyers d'erythropoïèse dans l'hypophyse de Cobaye gravide). Watrin (J.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 558-559.

Histological.—T. C. B.

Cachexia HYPOPHYSEOPRIVA. Zondek (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 1385; Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1297.

Report of a woman of 42 who had ceased menstruating when she was 34. She had gradually become thinner and finally severe cachexia developed. She now weighs 30 kg. The blood pressure is low; metabolism is much retarded; the thyroid cannot be felt; when extra doses of water or salt are ingested they are largely retained in the organism.—J. K.

The output of sugar from the LIVER as affected by C_H and minimal EPINEPHRIN. Snyder (C. D.), Martin (L. E.) & Levin (M.), Am. J. Physiol. (Balt.), 1922, **62**, 442-458.

The reverse action of minimal amounts of epinephrin has been demonstrated for the portal-venous system of the terrapin's liver. The present paper discusses how the output of sugar from the liver under similar conditions is affected. The same method was used as in the other experiments. The output of reducing substances per unit of time in the venous outflow is greater for the solution of lower pH, and less for the solution of higher pH. When minimal effective amounts of adrenalin are added to the perfusion fluid the minute-volume flow is less for solutions of higher pH, and greater for solutions of lower pH. This is due to the effects of adrenalin on vascular caliber and hence on intensity of irrigation rather than to a specific "epinephrin reversal."—T. C. B.

Evolution of the endocrine islands of the PANCREAS (L'évolution des îlots endocrines du pancreas). Aron (M.), Arch. d'anat., d'histol. et d'embryol. (Strassb.), 1922, **1**, 71-107.

The pancreatic islets should be distinguished into those of Laguesse and of Langerhans. In the embryonic pancreas the former appear first, and are regarded as the homologue of, and have a similar origin as, hepatic tissue; their physiological significance is still obscure. The islets of Langerhans appear later; their appearance is concomitant with the establishment of the glycogenic function of the liver. Morphological difference (staining reactions, etc.) are described between the 2 sets of islets in the 4 animals investigated (sheep, pig, guinea pig, and man).—Physiol. Abst., **7**, 448.

The relations between acids and bases and TETANY with special observations on the rôle of the phosphoric acid ion (Uber die Beziehungen von Säure und Alkali zur Tetanie mit besonderer Berücksichtigung des Phosphorsäureions). Elias (H.), Wien klin. Wchnschr., 1922, **35**, 784-786.

Many German authors think that disturbed acid-base regulation is the most important cause of tetany, but Elias confirmed the results of others, especially American investigators, who state that this factor is not important. The question of the treatment of tetany with acids or alkalies is not yet settled. Four facts, however, seem to have been established: (1) large quantities of acids increase in man and animal the irritability of the nerves; (2) small doses decrease this irritability; (3) alkalies increase the irritability; and (4) the PO_4 ion increases nervous irritability in normal and in tetanic subjects.—J. K.

The response of the submaxillary glands of the albino rat to THYRO-PARATHYROIDECTOMY and to PARATHYROIDECTOMY. Hammett (F. S.), Am. J. Anat. (Phila.), 1922, **31**, 103-107.

Using the "gentled" stock from the Wistar colony of albino rats, Hammett found that removal of the parathyroid glands results in a marked increase in the size of the submaxillary glands. The same result does not follow thyro-parathyroidectomy. Hence the enlargement cannot be attributed to any local irritation produced by the operative procedure. As a possible explanation it is suggested that the hypertrophy or hyperplasia is a response to an increased functional activity induced by the increased neural irritability resulting from the removal of the parathyroids.—W. J. A.

Three total THYRO-PARATHYROIDECTOMIES in the dog, with special observations concerning respiratory perturbations (Tres tiro-paratiroidectomias totales en el perro, con observacion especial acerca de las perturbaciones respiratorias). Ocaranza (F.), & Macedo (J. P.), Rev. mex. de biol. (Mexico, D. F.), 1922, **2**, 268-286.

In general the classic picture of thyro-parathyroid deficiency was noted. It is commonly stated, however, that the temperature falls immediately after this operation and that within 24 hours it notably ascends. In the first of the experiments reported hypertonia appeared 48 hours after the operation. In the second hypertonia appeared a few hours after the operation and, the next day, hypothermia. In the third experiment there was no hypertonia. The authors believe that vomiting, diarrhea and sialorrhea are not constant manifestations, but that tachycardia, hypertension, dilation of the pupils and congestion of the conjunctiva are characteristic. The respiratory disturbances in the three experiments were very similar. The primary phenomena consisted of polypnea, augmentation

of the amplitude of respiration, arrythmia, alternating respiration, brusque inspiration and prolonged expiration, this latter at times consisting of two convulsive efforts, the whole picture resembling that following double vagotomy. The tachycardia, with systolic augmentation and hypertension, the dilation of the pupils and the irritation of the conjunctiva, led the authors to think that the thyro-parathyroidectomized subject is in a state of sympatheticotonus.
—W. H.

(PARATHYROID) Relation between the chemical processes in the body and TETANY (Ueber die Beziehungen des Chemismus des Organismus zur Tetanie). Orgler, Deutsche med. Wchnschr (Berl.), 1922, **48**, 1008-1010; 1037-1038.

A review of the literature on chemical studies of the blood, urine and organs in tetany. Not only are calcium and phosphorus metabolism important but the excretion of comparatively large doses of acetone, the presence of guanidine in the urine and the large quantity of this substance in the stools must be explained. Most publications are of little value because they deal with only a small number of patients and because in the estimation of calcium inexact methods have been largely used, such as Wright's or Bang's method. The method of deWaard is better. All authors do not agree whether the phosphorus content of the blood is normal in tetany. Although tetania parathyreopriva, guanidine tetany and tetany of infants are not identical, they all improve when large quantities of calcium are ingested. The low calcium content of the blood probably causes the increased irritability.—J. K.

Influence of endocrine gland substance on morphogeny. Feeding tadpoles with PARATHYROIDS (Versuche über den Einfluss endokriner Drüsensubstanzen auf die Morphogenie). Schulze (W.), Arch. f. Entwcklngsmechn, d. Organ. (Berl.), 1921, **48**, 489-504.

The report deals with the results of feeding fresh bovine parathyroids, parathyroid extract (Freund-Redlich) and accessory thyroid (parathyroid?) tablets (Freund-Redlich), alone or in connection with **thyroid, testicular** and **ovarian** tissue, to 150 Rana fusca and 8 Bombinator pachypus larvae in different stages of development. Body measurements were made under light anaesthesia. The size of the thyroid, **thymus, pineal** gland and **hypophysis** was determined in some cases. Many animals were fixed and sectioned serially for histological study. The author found that fresh parathyroid produced (after an initial nonspecific acceleration in growth) no influence on development or metamorphosis. The parathyroid tablets accelerated metamorphosis but decreased the rate of growth, giving results similar to those produced by feeding fresh thyroid gland. Twenty-six references are given.—A. T. R.

(PARATHYROID) The influence of meat diet on experimental TETANY. Sinelnikov (E. I.), Russ. J. Physiol., 1922, **4**, 18-33.

Raw meat diet has no effect on **thyroidectomized** dogs, but increases the symptoms of tetany in **parathyroidectomized** dogs. The galvanic action in a normal dog was C.C.C.-2·0 milliamps, A.C.C.-2·8, A.O.C.-3·0, C.O.C.-5·6; after parathyroidectomy it changed to 1·4, 2·2, 2·8 and 2·8, and each time about 6½ hours after administration of 400 gm. of raw meat it was 0·4, 0·9, 0·9 and 1·4, respectively; c-tetanus was produced in the latter case with 2·0 m.a. and a-tetanus with 4·6 m.a. The active substance is soluble in water; boiled meat has no effect. Liebig's extract (4·5 gr. per kilo internally) causes severe convulsions. Guanidine, methylguanidine, carnitine and ablitine were found to be the active principles.

—Physiol. Abst., **7**, 445-446.

(PARATHYROID) Post-operative TETANY and pregnancy (Post-operatieve tetanie en zwangerschap). Stenvers (H. W.), Nederl. Tijdschr. v. Geneesk (Haarlem), 1922, **66** (II), 1049-1054.

Double strumectomy was performed on a woman in two operations. Immediately after the second operation she had a very severe attack of tetany. Large doses of fresh parathyroid were followed by good results. Transplantation had a very good effect, though spasms were still observed, especially during menstruation. Pregnancy five years later had a splendid influence, although some symptoms reappeared during the period of lactation. The author believes that this case proves that the general opinion as to the danger of tetany in pregnancy is unfounded.—J. K.

Tumors of the PARATHYROIDS and their relation to osteomalacic diseases of bone (Uber Epithelkörperchentumoren und ihre Beziehungen zu den osteomalacische Knockenerkrankengen). Strauch (B.), Frankfurt Ztschr. f. Path. (Weisb.), 1922, **28**.

The author discusses the possible relation to the incretory glands of diseases in which calcium metabolism is disturbed, such as rickets, osteoporosis, puerperal, senile and hunger osteomalacia and osteitis fibrosa. Some of the relations of the **gonads, thyroid, thymus, suprarenals, hypophysis** and parathyroids to the osteomalacic diseases are discussed. He reports a case of puerperal osteomalacia in a woman aged 27 years which terminated fatally three months after delivery. In addition to the generalized bone softening, tumor 4.8x3.2x3.5 cm., presumably involving the left internal parathyroid, was found. No other parathyroids were seen. In addition to several cystic spaces filled with clear fluid the parenchyma was composed of two types of cells, the principal, or basophilic cells, and groups of acidophilic cells. The cells were arranged in strands and an occasional follicle formation, i. e., not

essentially different from normal. Strauch was unable to make out any significant changes in the other glands of internal secretion. He refers to a number of similar cases with parathyroid tumor and bone softening reported in the literature and also to cases with parathyroid enlargement without bone changes. It is also known that marked softening of the bones may occur without demonstrable changes in the parathyroids. On this account the author concludes that tumors of the parathyroid give very little information regarding the causes of bone softening. They, however, add further evidence to the relationship between the parathyroid function and calcium metabolism.—S. S. (D. M.)

Tumors of the PINEAL gland (Die Zirbel und ihre Tumoren in ihrem funktionellen Einfluss). Askanazy (M.), Frankfurt Ztschr. f. Path. (Weisb.), 1921, **24**, 58-78.

The author reviews some of the theories of the function of the pineal gland and summarizes the information concerning its function that has been obtained from a study of its tumors. He reviews 11 cases of tumor, 8 of which were certainly teratomata, one probably a teratoma, one a chorio-epithelioma and one a glioma. These groups when occurring in males before the age of puberty were usually associated with precocious sexual development. The evidence of anatomical, clinical and experimental work to date favors the conception that the pineal gland functions usefully throughout life.—H. L. J. (D. M.)

The extirpation of the PINEAL gland and its influence on the HYPOPHYSIS (L'extirpation de la glande pinéale et son influence sur l'hypophyse). Urechia (C. I.), & Grigoriu (C.), Compt. rend Soc. de biol. (Par.), 1922, **87**, 815-816.

After removing the epiphysis from a great number of cocks the authors succeeded in maintaining two alive for 8 months. At first there was an involution of secondary sex-characters, but later development was rapid. Eight months after the extirpation of the pineal the animals were sacrificed. They appeared no different from the controls of the same generation. The weight of the testicles was the same as that of the controls, but microscopically there was a greater development of interstitial gland. The hypophysis was much larger in the animals that had been operated upon, with hypertrophy of the pars nervosa. Its structure indicated a hyperfunctional state.

—T. C. B.

The histology and physiology of the human PINEAL gland (Zur Histologie und Physiologie der menschlichen Zirbeldrüse). Walter (F. K.), Ztschr. f. d. ges. Neurol. u. Psychiat. (Berl.), 1922, **74**, 314-330.

Correction of Endocrinol., 1922, **6**, 910.—A. T. R.

SECRETIN studies (Etude sur la sécrétine). Djenab (K.), Ann. de méd. (Par.), 1922, **12,** 475-479.

Brief report of some work with rabbits which showed that secretin is partly destroyed by the liver, and that diet has an influence on the activity of the substance.—F. S. H.

Comparative studies of the activity of SECRETINS of the digestive tract (Vergleichende Untersuchungen über die Wirkungstärke der Secretine des Digestionstractus). Haramaki (K.), Biochem. Ztschr. (Berl.), 1922, **129,** 503-506.

All parts of the gastric mucosa produce secretin. Extracts from fundus, duodenum, rectum, colon and jejunum show secretin activity. The latter is a bit the weaker. Administration by mouth gives less reaction than does intravenous injection. Dogs were used in the experiments—F. S. H.

Influence of SECRETIN solutions on intestinal motility (Ueber den Einfluss von Secretinlösungen auf die Darmmotilität). Haramaki (K.), Biochem. Ztschr. (Berl.), 1922, **129,** 128-133.

The injection of histamine and spinach secretin into the ear-vein of a rabbit so prepared that direct observation of intestinal movement could be made was followed by intestinal peristalsis.—F. S. H.

The effect of SPLENECTOMY on integration of muscular movements in the rat. Macht (D. I.) & Finesilver (E. M.), Am. J. Physiol. (Balt.), 1922, **62,** 525-530.

Rats were trained to walk on a rope. It was found that extirpation of the spleen did not interfere with the coördination of the muscles or the running time of the animals. If anything, both were improved.—T. C. B.

The SPLEEN as an incretory organ (La rate envisagée comme glande à sécrétion interne). Stern (L.), Rev. suisse de méd., 1922, No. 25 (June); abst., Arch. méd. belge (Brux.), 1922, **75,** 816.

Stern, in collaboration with Rothlin, found in the spleen and in the blood of the splenic vein a substance, "liénine," that augmented both the tonus of the smooth muscle fibers and their sensitiveness to adenalin. Experiments were performed to demonstrate that, due to liénine deficiency, extirpation of the spleen caused the stimulating power of the blood on the vessel walls to diminish and the normal tonus of the smooth muscle fibers to change. Examination of the former did not give conclusive results, the factor being too variable even in the same subject. Alteration of the tonus of the smooth muscle fibers was studied indirectly by examination of the action of adrenin in animals before and after splenectomy. In the dog and

cat splenectomy did not modify the sensitiveness to adrenalin, but in the rabbit it took very large doses to give a pressor reaction equal to that previously obtained, although in the splenectomized animal the blood pressure remained as high as in the normal animal.

—R. G. H.

Status THYMICOLYMPHATICUS. Estill (R. J.), Proc. Kentucky State M. Ass., October 16-19, 1922.

A history of frequent severe colds with wheezing in the chest should make one suspect status lymphaticus, likewise the presence of enlarged tonsils with hyperplasia of the faucial and pharyngeal lymphatic tissue and enlarged lymph glands in infants under 2 years of age. It is probable that a complete examination of children under 2 years of age would show that status lymphaticus is more common than is believed to be the case. A roengen-ray examination of the chest should be made of every child giving a history of frequent colds or attacks of wheezing in the chest. Except in cases of sudden death in new-born infants and in neglected cases, the roentgen ray offers a very favorable prognosis in status lymphaticus.

—J. Am. M. Ass., **79**, 1793.

Status THYMICOLYMPHATICUS in infancy. Kohlbry (C. O.), Proc. Minnesota State M. Ass., October 12-14, 1922.

Kohlbry's patients were infants, the ages varying from 1 to 9 months. None had had any earlier illness. They all died with the first infection. Evidence of infection of comparative mildness was present in every case—an upper respiratory affection described as a cold. These infections were not accompanied by any considerable amount of fever. The illnesses were of short duration, three children having been sick only three days, while the others had had a cold for from one to two weeks before, with none but the local symptoms. Evidences of a pathologic condition in the thymus were found in all. Three patients showed stridor, and two showed, in addition, a dyspnea which was probably cardiac in origin. There was a definite roentgenographic shadow, such as is generally considered to be due to an enlarged thymus, in the only two cases submitted to roentgen-ray examination. In one case, a thymic area of dullness was obtained on percussion. The postmortem examination showed that the thymus weighed 13 gm. or more, the largest weighing 27 gm. There were hemorrhages into the gland in four of the five cases. Lymphoid hyperplasia was found elsewhere in the body in four cases, and was most evident in the mesenteric glands and the solitary follicles of the intestines. Sudden death was conspicuous in three cases. This occurred practically without warning. Evidence of a systemic disease was not lacking, as is shown by hemorrhages elsewhere. Two cases showed large hearts, with symptoms of cardiac dilatation in addition.—J. Am. M. Ass., **79**, 1792.

Serous-ferment perturbation and histological modifications of the principal digestive organs after THYMECTOMY (Perturbamento siero fermentativo e modificazioni istologiche dei principali organi digestivi in seguito a timectomia). Ruggeri (E.), Folia med. (Napoli), 1922, **8**, 225-233; 275-280.

After total ablation of the thymus in the pigeon a few symptoms appear, as post-operative weakness, with later exaggerated appetite, and more fluid and acid excreta. The enzyme production was temporarily perturbed. The complement titre was diminished and thymectomized animals were easily infected. A histological study was made of some organs related to the digestive apparatus. Diminution of glycogen in the liver and changes in the mitochondria of the pancreas and duodenum were found.—G. C.

(THYROID) Pregnancy in a myxoedematous woman (Grossesse chez une myxoedemateuse). Audebert & Claverie, Bull. Soc. d'obst. et de gynéc. (Par.), 1921, **20**, 79-80.

A case report illustrating the diminution of hypothyroid symptoms during pregnancy. The latter is associated with a hypertrophy of the thyroid, and almost always with an increased function. This explains the autotherapeutic effect exerted upon myxoedema by pregnancy.—E. N.

(THYROID) Myxedema and imbecility (Myxoedème et imbécilité). Ballif (L.), Bull. et mém. Soc. de neurol., psychiat. et psychol. de Jassy, 1921, **3**, 1-2 (September).

Presentation of a case. The important factor in this case is the fact that patient had a sister with goiter. Attention is drawn to diversity of manifestations of thyroid disorders.—F. S. H.

Action of iodine and of iodides upon the THYROID of healthy and tuberculous guinea pigs. Bezançon (F.) & de Jony (S.-I.), Rev. tubercul., 1920, **1**, 36-39; Abst. Bact., **5**, 165.

The thyroid gland of the normal guinea pig weighs 0.05 to 0.07 gm. KI or Gram's iodide causes the vescicles to distend and the epithelium to flatten out, but with an absence of interstitial hyperplasia; the reaction is more pronounced with subcutaneous injection than with mouth ingestion. With iodized water or oil there is a distinct and marked hyperplasia, increasing in weight to 0.36 gm. at times. The gland in a tuberculous pig resembles that of a tuberculous person. Iodine has no influence on the course of the disease. The gland tends to become normal, the epithelium being entirely normal. KI on the other hand causes an intense vascular congestion.
—Chem. Abst., **16**, 3975.

THYROTOXICOSIS. Blackford (J. M.), Surg., Gynec. & Obst. (Chicago), 1922, **34**, 185-188 (February).

The treatment of exophthalmic goiter is essentially surgical. Early diagnosis is important. The mortality from removal in nontoxic or mildly toxic cases is almost zero in competent hands, and the net results are satisfactory. The cardiac reserve of the patient is nearly always good enough to withstand operation. The bulk of surgical mortality occurs in the badly toxic cases, not in cases of extreme cardiopathy.—E. N.

The THYROID problem (Untersuchungen zur Schilddrüsenfrage). Breitner (B.), Wien. klin. Wchnschr., 1922, **35**, 969-971.

General discussion.—J. K.

(THYROID) Problems of Graves' disease (Problemstettung beim morbus Basedowi). Breitner (B.), Mitt. a. d. Grenzgeb. d. Med. u. Chir. (Jena), 1922, **35**, 637-650.

There is a very close relation between the **sexual organs** and the **thyroid.** Physiological hyperfunction of one causes physiological hyperfunction of the other. Graves' disease is more frequent in women, due to menstruation, pregnancy and childbirth. This may account for the beginning of Graves' disease at the time of first menstruation. In man, too, it is not unusual to find sexual disorders as important factors in the pathogenesis of Graves' disease. Generally hyperfunction of the sexual organs is the primary cause; primary hyperfunction of the thyroid is rare. The familiar form of Graves' disease, however, may be due to anatomical variations. Diseases giving rise to fever may cause increased absorption of the thyroid hormone, thus causing hyperthyroidism. The clinical picture depends upon the intensity of the symptoms, originating in the thyroid. Classical Graves' disease is caused by a combination of increased or decreased activity of the complete endocrine system. The theory that dysfunction of the thyroid causes Graves' disease is not accepted by Breitner. He remarks that it is impossible to prove the existence of this dysfunction. The author does not believe that the problems concerning exophthalmic goiter have been solved, but hopes by his theories to reduce the confusion now existing in endocrine literature.—J. K.

Studies on the condition of activity in endocrine glands. IX. Further evidence of nervous control of THYROID secretion. Cannon (W. B.) & Smith (P. E.), Am. J. Physiol. (Balt.), 1922, **60**, 476-495.

Cats under light ether anesthesia were used. Massage of the thyroid for 2 or 3 minutes causes increased rate of the denervated heart, reaching a maximum in from 30 to 60 minutes. Augmentation occurs in the absence of the **adrenals.** If the thyroid has been previously removed, stimulation of the cervical sympathetic trunk as it leaves the stellate ganglion also augments the denervated heart.

Sensory stimulation and asphyxia induce a brief augmentation after removal of the thyroids, due to adrenal and hepatic discharge. If the cardiac fibers from the stellate ganglion, and also the vagi are cut, stimulation of an afferent nerve (sciatic or brachial) will cause a primary increase due to adrenal secretion, followed by a more slowly developing thyroid effect. The same is true of asphyxia under similar conditions. Compared with vascular reactions as a test of thyroid activity this has the advantage of not requiring destruction of the upper portion of the central nervous system. In an addendum it is stated that these experiments were repeated in March and April with negative results, due to seasonal variations in iodine content of the thyroid.—T. C. B.

(THYROID) Lues hereditaria tardía: Endocrinopatías. Castex (M. R.) & Waldorp (C), Prensa méd. argentina (Buenos Aires), 1920, **7**, June 10.

Graves' disease is produced in a large number of cases by late hereditary lues. Familial cases are seen in syphilitic families.

—B. A. H.

Unilateral tumefaction of the THYROID, breast and testicle in a soldier with war traumatic neurosis (Tumefazione unilaterale della tiroide, della mammella e del testicolo in un soldato con nevrosi traumatica di guerra). Chimisso (L.), Folia med. (Napoli), 1922, **8**, 481-496.

An interesting clinical case in which the syndrome consisted in paralysis and anesthesia of the right arm, lagophthlithalmus, exophthalmus, and mydriasis on the right, swelling of half the thyroid, testicle and breast of the same side, and analgesia of the testicle. The etiology consists in a traumatic neurosis from war shock, which affected only the right sympathic.—G. C.

THYROID gland and tuberculosis (Corps thyroïde et tuberculose). Coulaud (E.), Thèse de Par., 1922; abst., Presse méd. (Par.), 1922, **30**, 992.

There has been a tendency of recent years to consider that thyroid deficiency leads to predisposition to tuberculosis. After having studied the function of the thyroid in connection with the immunity phenomena, the author concluded that there is no ground for this hypothesis. He tubercularized hypothyroid rabbits, but these animals lived even longer than the controls. Histologically the thyroid in the tuberculous subject appeared to function normally. Clinical observations confirm this theory; patients with simple goiter, with Graves' disease, and with myxedema are tuberculous only exceptionally. But in women times of physiological hyperthyroidism coincide with periods of lowered resistance; tuberculosis is most active during menstruation, pregnancy and the menopause. Coulaud cites some

curious instances in which tuberculosis seemed to become manifest under the influence of thyroid opotherapy. **Ovarian** opotherapy, which is often used to moderate thyroid function, seems capable, in a large number of cases, of contributing to the reestablishment of allergy.—R. G. H.

Action of x-rays on the THYROID of the adult rabbit (Action des rayons X sur le corps thyroïde du lapin adulte). Coulaud (E.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 1014-1016.

Histological description of the thyroid after irradiation of various intensities and at various times after irradiation has been discontinued.—T. C. B.

(THYROID) Clinical types of goiter and their management. Elliott (C. A.), Med. Clin. N. Am. (Phila.), 1922, **5**, 1623 (May).

This author says: "We have not observed the definite and lasting results which would stamp these agents as all sufficient in the treatment of hyperthyroidism," but it is stated that perhaps these agents have not been perfectly applied. "In general it must be admitted that radium and x-ray may be sufficient in any given case and that they are useful in reducing hyperthyroidism preliminary to operative interference." In selected cases of toxic goiter radium or x-rays may be indicated and in exophthalmic goiter they may be advisable preliminary to a subtotal thyroidectomy.

—J. Radiol., **3**, 509.

The quantity of iodine in THYROID extracts (Sur le dosage de l'iôdide dans les extraits thyroïdiens). Fabre (R.) & Penau (H.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 1026-1028.

(THYROID) Methods and technic of goiter operations (Ueber Methodik und Technik der Kropfoperation). Flörcken (H.), Beitr. z. klin. Chir. (Tübing.), 1922, **127**, 85-97.

See Endocrin., **6**, 731.

Iodine contents of the THYROID of the Japanese. Fukushima (T.), J. Jap. Soc. Int. Med., 1921, **9**, No. 5; Jap. Med. World, 1922, **2**, 45.

The average total weight of the thyroid of the Japanese is ⅓ that of the European. The distribution of I in the bilateral lobes occurred evenly; the average was 0.81 mg. in the left and 0.811 mg. in the right, per 1.0 gm. fresh glands. The Japanese thyroids contained, comparatively, remarkably larger amounts of I, probably because of the rich fish diet.—Chem. Abst., **16**, 3951.

Physiology of the frog's THYROID (Contributo allo studio della fisiologia della tiroide della rana). Gayda (T.), Arch. di fisiol. (Firenze), 1922, **20**, 209-224.

Thyroid extirpation and administration experiments on frogs (18 in all, including controls) were performed. There was no appreciable morphological or functional difference in the results following thyroid extirpation in winter and summer frogs. As an immediate consequence of the operation the heat production gradually diminished to the time of death. This was not very considerable in the winter frog (14 to 28%); in the summer animal it was more marked (31 to 42%). In every case the heat production value changed in one way only until the death of the animal, some months after the extirpation. Ingestion of sheep's thyroid into the normal or thyroidectomized frog never produced any phenomenon resembling hyperthyroidism. The heat production either did not vary, or showed a slight and transitory increase of not more than 10%, and lasted not more than 2 or 3 days. Feeding by mouth either sheep's thyroid or flesh produced no marked differences from normal. It is concluded that the frog's thyroid is not of the same importance in heat regulation as that of homothermal animals, and in the frog is of more importance in the developing animal than in the adult.

—A. T. C.

Studies of the THYROID apparatus. VIII. On the alleged exogenous source of the poisons giving rise to tetania parathyreopriva. Hammett (F. S.), Am. J. Physiol. (Balt.), 1922, **63**, 151-154.

Two groups of 24 white rats each were put on a diet, one group exclusively meat, the other exclusively lettuce. After 4 days they were all parathyroidectomized. Of those on a meat diet, 37.5% died in 48 hours; of those on a lettuce diet, 58.4% died in 48 hours, all of acute tetany. The rats with a low exogenous metabolism of protein had the greatest mortality, and the author thinks this disproves the conclusion of Luckhardt and Rosenbloom that "the" source of the poison responsible for tetany is of exogenous origin; it is only "a" source.—T. C. B.

(THYROID) A possible factor in the increasing incidence of goiter. Hayhurst (E. R.), Science (N. Y.), n. s. **54**, 131.

The suggestion is made that the increasing incidence of goiter is due to the use of purified NaCl as a condiment instead of sea salt as in former times.—F. A. H.

(THYROID) Alteration of metabolism after chronic administration of morphine (Ueber Veränderungen des Stoffwechsels nach chronischer Morphinzufuhr). Hildebrand (F.), Archiv. f. exper. Path. u. Pharmakol. (Leipz.), 1922, **92**, 68-95.

From the results of respiration experiments obtained on four rats (by means of Rohde apparatus) the author concludes that there is an analogy between the effects of thyroidectomy and the chronic administration of morphine. In both cases there was a decrease of

the oxygen consumption for 3-4 weeks and an increase of the respiratory quotient (perhaps due to an increased combustion of carbohydrates). In both cases the administration of thyraden was followed by a rise of the low basal metabolism and by a decrease of the respiratory quotient. The thyroidectomized and the chronically morphinized rats showed a diminished sensitiveness to lack of oxygen. The sensibility for morphine increased after administration of thyroid substance and decreased after thyroidectomy.

—R. W.—A. B.

(THYROID) Experimental study of the pathogenesis of exophthalmos. Idzumi (G.), Tokyo Iji-Shinshi, 1922, No. 2278 (May); abst., Jap. Med. World, 1922, **2**, 296.

Idzumi discovered that functional derangement of the epithelial body results in swelling of the thyroid. He extirpated the epithelial bodies of a guinea pig and fed it with calcium and phosphorus. The animal thus fed showed a swollen thyroid. Characteristics of the teeth and microscopical findings of the thyroid both showed manifestations similar to those in human cases of exophthalmos.—R. G. H.

(THYROID, PARATHYROID, THYMUS) Branchial derivatives in turtles. Johnson (C. E.), J. Morphol. (Phila.), 1922, **36**, 299-329.

The development of the branchial derivatives was studied in turtles of the genera Chelydra, Chrysemys, and Trionyx. The results are of interest principally to the embryologist.—W. J. A.

The THYROID gland and sensibility of tuberculous animals to tuberculin (Glande thyroïde et sensibilité des animaux tuberculeux envers la tuberculine). Kepinow (L.) & Metalnikow (S.), Compt. rend. Soc. de biol. (Par.), 1922, **87**, 210-213.

Having previously studied the rôle of the thyroid in serum anaphylaxis, the present paper deals with an allied phenomenon—the reaction of tuberculous animals to tuberculin by a rise in temperature. The thyroid was removed from 4 guinea pigs, and 4 others were kept intact as controls. All were inoculated subcutaneously with a virulent culture of tubercule bacilli 8 days after the operation. A month later they were injected subcutaneously with tuberculin, some lethal, others not. The controls reacted by an elevation of temperature, while the thyroidectomized animals showed no appreciable rise. Those receiving a lethal dose of tuberculin, whether experimental or control, died. It would seem, then, that the rise of temperature, classed among the facts of anaphylaxis, is bound up with the thyroid function, while the purely toxic character of the tuberculin is not. In another series of animals the effort was made to confer a passive thermic sensibility by injecting the serum of tuberculous guinea pigs, thyroidectomized and non-thyroidectomized, into normal guinea pigs. All the non-thyroidec-

tomized animals reacted promptly, while the thyroidectomized did not respond. None of them died. It is assumed that only the thermic action is transmitted passively. The serum of thyroidectomized animals transmits neither the thermic sensibility nor the toxic effects.—T. C. B.

(THYROID) Treatment of goiter with parenchymatous injections (Ueber die Behandlung des Kropfes mit parenchymatösen Einsprikungen). Krebs (G.), Deutsche med. Wchnschr. (Berl.), 1922, **48,** 898.

The author has injected about 1000 goiters with tincture of iodine. Only in vascular (especially) or cystic goiters were results obtained. To avoid thrombosis it is necessary to aspirate before injecting. If blood runs into the syringe the needle must be removed and the injection must be repeated in another part of the goiter. Ordinarily 5 to 8 injections are enough, but 20 may be necessary before good results are obtained.—J. K.

(THYROID) Atrophy of terminal phalanges in a rheumatic and sclerodermic patient with goiter, dying of tuberculosis (Atrophie des phalangettes chez une goitreuse rhumatisante et sclérodermique, morte tuberculeuse). Laignel-Lavastine & Coulaud (E.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46,** 1526-1530.

(THYROID) Causes of death in goiter (Uber die Bedingungen des Kropftodes). Lang (F. J.), Klin. Wchnschr. (Berl.), 1922, **1,** 2461-2464.

A discussion of the dangers caused by toxic and non-toxic goiters and the different ways in which they may be responsible for sudden death.—J. K.

(THYROID) Influence of the parenteral administration of protein on gaseous metabolism (Ueber den Einfluss der parenteralen Eiweisszufuhr auf den Gasstoffwechsel). Leimdörfer (A.), Biochem. Ztschr. (Berl.), 1922, **133,** 409-416.

These studies show that parenterally administered protein produces an increase in the oxidative processes which is accompanied by a rise in temperature. If the latter does not occur there is no change in gaseous metabolism. A discussion of the rôle of the thyroid and chemical heat regulation is given.—F. S. H.

Mental anorexia and the THYROID. Lévi (L.), Encéphale (Par.), 1922, **17,** 507-516 (October).

Lévi reports some cases of mental anorexia in which thyroid treatment restored conditions to normal. The appetite returned and the three women gained in weight. Analysis of the cases shows absence of appetite from thyroid insufficiency. On this had

become superposed a mental condition aggravating the anorexia and perpetuating it.—J. Am. M. Ass., **79**, 1961.

The red sign of the THYROID (Sur la signe de la tache rouge thyroïdienne). Marañón (G.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1635-1641.

(THYROID) Intravenous chemical treatment of Graves' disease and goiter (Eine intravenöse Chemotherapie der Basedowschen Krankheit und des Kropfes). Mendel (F.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 896-897.

The administration of very small doses of iodine in Graves' disease, as recommended recently by some German authors, is not a new therapy. More than 10 years ago the author described a treatment in which NaI and atoxyl were given together. Every 2 days, and in light cases twice a week, 2 cc. of the following solution is injected: atoxyl, 1 gm.; NaI, 8 gm.; water, 40 cc. This combination can be bought in ampules and is called "jodarsyl." In simple goiters good results are also seen, although improvement is not so rapid as in Graves' disease.—J. K.

(THYROID) Development of goiter in children (Die Entwicklung des Kropfes bei Kindern). Messerli (F. M.), Rev. méd. de la Suisse Rom. (Genève), 1922, **42**, 176; abst., Monatschr. f. Kinderh. (Leipz.), 1922, **23**, 555.

From the standpoint of prophylaxis it is important to determine the age of the incidence of goiter. The author's studies on school children in a goitrous town showed that the goiter preceded their enrollment in school, hence prophylaxis should have been instituted previous to this time.—R. G. H.

HYPERTHYROIDISM. Murray (G. R.), Brit. M. J., 1922, **i**, 905-908 (June 10).

A general article. Murray feels that surgery is indicated in cases which show pressure symptoms or evidence of rapidly advancing toxic myocarditis. In any case he believes that medical treatment should have a full trial for six months before surgery is considered.
—F. C. P.

Contribution to the morphologic study of the THYROID gland in Emys europaea. Naccarati (S.), J. Morphol. (Phila.), 1922, **36**, 279-297.

A detailed study of the macroscopic anatomy, circulation, innervation and histology of the thyroid in two turtles, Emys europaea and Testudo graeca. The steps in the technique of Galeotti's staining method, which the author highly recommends, are detailed. There are two colored plates.—W. J. A.

(THYROID) Experimental studies on the so-called Kocher's blood features in exophthalmic goiter. Ohhara (H.), Nisshin Igaku, 1922, **11**, No. 8 (April); cit., Jap. Med. World, **2**, 300.

The sensitizing action of THYROID extract for adrenaline. Ono (S.), Jap. Med. World, 1922, **2**, 157-160.

Using isolated organs, Ono found that an active principle of thyroid extract sensitizes the heart of the toad and the blood vessels of the cow for the action of adrenaline.—Chem Abst., **16**, 3976.

Iron in the blood of THYROIDECTOMIZED animals (Sur la teneur en fer du sang des animaux ethyroïdes). Parhon (M.), Endocrin. e patol. costituz. (Roma), 1922, **1**, 39.

In 6 sheep, thyroidectomized at the age of 6 weeks, the author found a diminution of iron in the blood, thus causing retardation of internal oxidation.—B. A. H.

Differential diagnosis of diseases of the THYROID gland. Phillips (J.), Canad. M. Ass. J. (Montreal), 1922, **12**, 318-327.

Anaphylaxis and THYROID (Anafilassi e tiroide). Pistocchi (G.) Pathologica (Genova), 1922, **14**, 717-718 (November).

Lanzenberg and Képinow's studies on the effect of partial thyroidectomy in reduction or prevention of anaphylactic crises agree with the previous publication of the author (1920). Képinow states that since in the transmission of passive anaphylaxis thyroidectomy is indispensable in the transmitting animal, the thyroid must elaborate the substances determining the shock. The author is inclined to believe, however, that the thyroid has an indirect value, that through thyroidectomy the whole organism changes and may become unable to prepare the substances necessary to anaphylaxis.
—G. V.

(THYROID) New medical treatment of goiter (Nouveau traitement médical du goitre). Regnault, Soc. de méd. de Par., 1922, Nov. 10; abst., Presse méd. (Par.), 1922, **30**, 1011.

The author gave 30 cgm. of thyroid extract and 3 mg. of parathyroid extract 3 times in 24 hours. This treatment was kept up for 3 weeks, followed by 8 days of rest. Good results were obtained in simple goiter, some cases of exophthalmic goiter and in thyroid insufficiency.—R. G. H.

Treatment of goiter by THYROID and PARATHYROID extracts (Traitement du goitre par les extraits thyroïdes et parathyroïdes associés). Regnault (F.), Soc. de pathol. comparée, 1922, July 11; abst., Presse méd. (Par.), 1922, **30**, 652.

Regnault, led to the use of this treatment by considerations of comparative anatomy, obtained some results which should encourage

investigators to attempt verification. After being assured of the condition of the circulatory system of the patient he prescribed 10 centigram pills of thyroid extract and 1 mg. wafers of parathyroid. The author advocates the administration of 1 pill and, three minutes later, 1 wafer before a meal (always watching the heart closely) for three or four days; then 2 pills and 2 wafers morning and evening, and, finally, 3 pills and 3 wafers, with a rest of 8 days every 3 weeks.—R. G. H.

(THYROID) The surgical treatment of exophthalmic goiter. Romanis (W. H. C.), Lancet (Lond.), 1922, **ii**, 471-475.

Only those patients are included in this article who showed rapid and definite cardiac changes, eye changes and typical findings on microscopic examination. Operative mortality is usually due to acute thyroid intoxication and occurs in the first 48 hours, the symptoms being a rapidly increasing pulse, fever, restlessness, delirium and acetonuria. Under local anesthetic this seems to be less—in the last group of 250 operations the mortality was 2.4%. In mild cases a period of observation may result in complete disappearance of the symptoms; more often surgical measures must be resorted to. In patients with maniacal, delusional or melancholic symptoms thyroidectomy offers less striking results. Implantations of radium have often given better results. Preference is given to local anesthetic preceded by morphia and hyoscine. One lobe, the isthmus and from a third to a half of the other lobe should be removed at operation. A working plan is to leave a fragment of thyroid about the size of one normal lobe. There was no tetany in this series. The remainder of the patients were improved in condition, and in the course of 3 to 4 months the pulse came down to 80 to 90. Often some cardiac dilatation remained. The tremor and irregularities of the pulse disappear and the exophthalmos recedes but does not disappear. The best results are obtained before cardiac changes have taken place. The basal metabolic rate drops from +40 to 80 or more to something over +25 in a few weeks.—R. E. K.

Isolation of the THYROID hormone (Versuche zur Isolierung des Schilddrüsenhormones). Romeis (B.), Biochem. Ztschr (Berl.), 1922, **132**, 97-111.

Normal thyroid glands of freshly slaughtered sheep were minced, mixed with 10 times the amount of hot saturated $Ba(OH)_2$ solution and cooked under a reflux condensor until no biuret reaction was given (12 to 14 days). The cooled extract was treated in 3 ways. The first method consisted in neutralizing with H_2SO_4 and filtering off the yellowish $BaSO_4$ precipitate. The filtrate and washings were concentrated on the water bath to a protein-free syrup. This material induced accelerated development of frog tadpoles, but slower than that caused by iodothyrin. The second method consisted

of precipitating the Ba from the hydrolyzed extract by CO_2 and making the reaction alkaline with Na_2CO_3. The $BaCO_3$ was removed by filtration and washed. The combined filtrates were concentrated and neutralized with acetic acid. The syrup was very active in promoting tadpole development, thus indicating that in neutralization with H_2SO_4 the greater part of the active principle is carried down with the $BaSO_4$. The third method consisted of neutralizing the $Ba(OH)_2$ with HC1. $BaC1_2$ remained in solution and the active part was precipitated out and filtered off after standing for several hours. Further purification was obtained by repeated solution in diluted NaOH and reprecipitation with acetic acid. Very small amounts of the dry precipitation sufficed markedly to accelerate tadpole development. Further purification was obtained by repeated extracting with 90% alcohol slightly acidified with acetic acid and evaporation of the alcohol from the filtrate. The final product was washed with water-free ether and petrol-ether. The product contained much iodine and appeared to be like thyroxin.—F. S. H.

Investigation on isolating THYROID gland hormones (Versuche zur Isolierung des Schilddrüsenhormones. 1. Tiel). Romeis (B.), Arch. f. Entwcklngsmechn. d. Organ. (Berl.), 1922, **50**, 410-467.

This is a report on 18 experiments in which a total of 805 tadpoles (mostly Rana temporaria) were used. It was found that an extract of the thyroid gland, purified, and having the albumin removed by several precipitations with absolute alcohol, causes in the tadpole experiment acceleration in development, but not the stimulation constantly noted on feeding with fresh thyroid gland. It is therefore a question whether this acceleration in development is to be considered as organically specific. The precipitate, rich in albumin, which comes down after the first alcohol precipitation causes a great stimulation, inhibits growth, and accelerates development. The purified substance from the alcohol extract, soluble in benzine, calls forth no acceleration in development. By extracting with 50% alcohol, acidulating with acetic acid and precipitating twice with acidulated 96% alcohol, it is possible to obtain from the fresh thyroid gland an alcoholic albumin-free extract fraction which causes stimulation, inhibits growth and accelerates development. The albuminous substances precipitated by acetic acid work the same way. The precipitates obtained by the first and second alcohol precipitation work only weakly (the first more than the second). The specific albumin-free extract portion, soluble in alcohol, is not soluble in benzine. It contains iodin. It may also be extracted from the fresh gland with 80-90% alcohol. The substance soluble in alcohol for the most part goes over into the acetone extract when acetone is used for dividing. But the division is not quantitative. By repeated operations the insoluble acetone portions causes inhibition of growth and acceleration of development. By shaking out the

acetone soluble extract with benzol, toluol, and trichlorethylen, the effective substance goes over into the extraction material only in traces or not at all. Even the substances separated from the extract with ether are not specifically effective when the shaking out occurs in aqueous solution in a neutral reaction and the extract obtained is once more taken up in pure ether after drying. The ether extract obtained in this manner contains cholesterin and a yellow unknown intermediate substance (probably corresponding to the "accompanying substance" of Wacker). Considerable numbers of effective substances go over into the ether extract when the extract in alcoholic solution is shaken out with ether. When this extract is dried and taken up in pure ether, the effective substance with a number of other substances remains insoluble. The substances (mostly cholesterin) dissolved in pure ether are not specifically effective. The residue containing iodin is for the most part soluble in neutral H_2O. The aqueous solution is very effective, also the scant precipitate which is soluble in weakly alkaline water. More abundant is the effective substance going over in the alcohol-ether-extract previously acidulated with H_2SO_4. The specifically effective substances are precipitated by a sulphuric acid reaction from the purified albumin-free extract by phosphotungstic acid. It goes into the solution with barium when the phosphotungstic acid precipitate is decomposed. In the barium phosphotungstic acid precipitate there remains behind a substance to be extracted with NaOH or NH_3, which at neutralization precipitates for the most part and in the tadpole experiment retards growth without at the same time accelerating development. The substances going over into the filtrate and which are not precipitated by the phosphotungstic acid are not specifically effective. The effective substance precipitated by phosphotungstic acid and freed by barium hydroxide is soluble in 90% alcohol. The methods used do not show iodin in these substances. In spite of this it calls forth in the tadpole experiment the typical thyroid gland activity. After dissolving several times in 90% alcohol, small amounts of a crystallized substance could be obtained from weak sulphuric acid solution, a substance which in the tadpole experiment caused stimulation, checking of growth, and acceleration of development. As the absence of iodin indicates, this substance does not correspond with Kendall's thyroxin. The effective substance is further precipitated from the albumin-free extract by sublimate from neutral solution. Sublimate sodium acetate precipitates best. Alcoholic sublimate solution is also good. The substances that are not precipitated have no specific efficacy. The substance is not precipitated out by acid reaction. An aqueous thyroid gland extract made albumin free with aluminum silicate with acid reaction affects, in the tadpole experiment, growth and accelerates development. The efficacy of accelerated development is clearly distinguished from the typical thyroid gland activity by the absence of stimulation. The specific effective

substance is by this method separated at the same time as the albumin bodies. By shaking out one of the extracts made albumin-free with alcohol according to the above method with aluminum silicate, the effective substance is absorbed by aluminum silicate. The substances not absorbed have little or no specific efficacy. The absorbed effective substance may be extracted from the absorption medium by means of NaOH or NH_3. The extract portion isolated in this manner is free from albumin, albumoses or peptones. It contains iodin. The substance obtained by neutralizing or acidulating this extract portion causes marked stimulation and moderate acceleration in development. Even the filtrate is still specifically effective. In the same manner as through aluminum silicate, the effective substance is adsorbed by animal charcoal. The filtrate has lost its specific efficacy. The substance adsorbed by aluminum silicate and dissolved in NaOH remains for the most part in the tube in dialysis through collodian membrane; but it is not albumoses. KIO_3, KI, $NaIO_3$, NaI and Lugol's solution in the tadpole experiment in dilutions of 1:50,000-1:500,000 cause neither acceleration of development nor retardation of growth. A stronger concentration is sometimes followed by death of the animal. Diiodtyrosin in only small doses (20-40 mg.) causes very distinct stimulation, acceleration in development, and checking of growth. The effect much resembles the symptoms appearing after strong thyroid gland feeding or administering of iodothyrin. In the very young Esculenta larvae the effect is much slower than with iodothyrin. Diiodtyramin, on the contrary, is weakly or not at all effective. The difference in the efficacy of diiotyramin and diiodtyrosin depends on the presence of the carboxyl group; by substituting for them the amino group the specific efficacy is more or less lost. By these experiments it is shown that the specific efficacy of the thyroid gland feeding in tadpoles may be brought forth by an extracted albumin-free substance from the fresh gland. This is effective even if there is no longer a trace of iodin; but of course its efficacy is doubtless increased by the presence of iodin in a certain form of combination which is still unknown. The substance is abiuret, sulphur free and does not give a Millon reaction. The negative result of the Millon reaction would in the iodin-containing substance not contradict the presence of diiodtyrosin. But the test is also negative in the iodin-free preparation. The negative result of the Adamkiewicz-Hopkins test, which it was possible to confirm in some preparations without a distinction between their efficacy and that of a positive Adamkiewicz-Hopkins reaction, points to the absence of tryptophan complexes, which is of interest in view of the Kendall thyroxin which is a tryptophan derivative. Whether the isolated substance in the present experiment corresponds to the in vivo secreted hormone of the thyroid gland will have to be proved in further experiments, especially since it has not

been shown that the results obtained in tadpoles may without restriction be carried over to higher vertebrates.—E. C. K.—A. T. R.

Influence of vertebrate hormones on invertebrates. I. Influence of THYROID feeding on development and growth of the flesh-fly (Colliphora vomitoria) [Experimentelle Untersuchungen über die Wirkung von Wirbeltierhormonen auf Wirbellose. I. Der Einfluss von Schilddrüsenfütterung auf Entwicklung und Wachstum der Schmeissfliege (Calliphora vomitoria)]. Romeis (B.) & von Dobkiewicz (L.), Arch. f. Entwcklngsmechn. d. Organ. (Berl.), 1920, **47**, 119-130.

The eggs on thyroid tissue at first develop more slowly than the controls (on muscle tissue), being delayed about 35 hours. The first appearance of the freely moving larva is delayed 25 hours. The maggots remain underdeveloped during the first day, but in the second half of the larval stage the experimental animals are accelerated so that before the pupa stage they have caught up with the controls. The metamorphosis into the chrysalis is delayed 35 hours, as is also the time when they commence to crawl. The thyroid fed pupae are normal to external appearances and slightly heavier in weight than the controls. The experimental adult flies can not be distinguished from the controls. Nineteen references are given.—A. T. R.

(THYROID) Roentgen treatment of toxic goiter. Rowe (E. W.), Nebraska M. J., 1922, **7**, 329 (October); abst., J. Radiol. (Omaha), 1922, **3**, 560.

The author sums up his conclusions as follows: Properly selected cases are as rationally treated by roentgen rays as by surgery. Adolescent toxic cases and early toxic cases yield most readily. Adenoma with toxicity yields less readily, but often gives brilliant results. Exophthalmic goiter shows the best results of all, and if roentgen treatment is faithfully carried out surgery is seldom required, while the results are as permanent. Malignancy is no contra-indication. Pfahler reports two cases permanently cured. There is no harm in the treatment and many patients are cured. There is no fear of operation, less likelihood of recurrence, and no scar on the neck. Three series may effect a cure. Sometimes six or eight are required. The tonsils when infected should, with other foci of infection, be treated. The tonsils may be treated at the same time by the roentgen ray with high probability of relief. Treatment should be given only by, or in cooperation with, an experienced clinician. The estimation of the basal metabolic rate in the selection of cases will determine the thyroid activity better than any other method. It will help also to visualize the progress of the patient and give a safe indication when treatment should be discontinued.—R. G. H.

(THYROID) Actual state of the goiter problem. (Estado actual del problema del bocio). Schmiedem & Hellwig, Arch. de med., cirug. y espec. (Madrid), 1922, **8**, 105-110.

Recent anatomical work has amplified our knowledge of endemic goiter. The study was directed to the plain and mountainous countries. In the latter were found patients having vestiges of adenomas, smaller vesicles, accompanied by a thick collodial substance, abundant parenchyma, much conjunctive tissue, and sparse vascular development. Weguelin supposes that these changes are due to the direct action upon the glandular epithelium of a toxic substance produced by the thyroid. The authors studied the action of alkaline iodides upon the thyroids of the dog, their experiments demonstrating that there is considerable dilution and increase of the contents of the vesicles or, it may be, increase of thyroid secretion. These results account for the prophylactic and curative action of iodine. Up to the present time goiter has been considered as a form of degeneration, but the authors believe it to be a condition of hypersecretion which is liable to lead to hyperthyroidism. Due attention should be given to iodine as a prophylactic in cases of goiter.—E. B

THYROID extirpation in tadpoles (Schilddrüsenexstirpation bei Froschlarven). Schulze, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 1263.

A very short note. In larvae of Rana fusca the anlage of the thyroid were removed a short time before metamorphosis. Metamorphosis was retarded; complete removal caused failure of further development. When thyroid was given to the animals that had been operated upon metamorphosis began much sooner than in the controls that had been operated upon.—J. K.

(THYROID) Conditions for the occurrence of goiter (Uber die Entstehungsbedingungen des Kropfes). Schwenkenbecker (A.), Klin. Wchnschr. (Berl.), 1922, **1**, 2457-2461.

A critical review of the theories as to the cause of goiter. None of these theories explains all the problems.—J. K.

(THYROID) Compression of the brachial plexus and the sub-clavicular blood-vessels by a goiter (Compression par un goitre du plexus brachial et des vaisseaux sous-claviers). Sézary (A.) & Bartet (P.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 1499-1502.

(THYROID) Relations between goiter and heart (Beziehungen zwischen Kropf und Herz). Steiner (O.), Mitt. a. d. Grenzgeb. d. Med. u. Chir. (Jena), 1922, **35**, 39-66.

In most cases the oppression of respiration in goiter does not seem to depend upon compression of the trachea. In patients with only very slight stenosis the feeling of oppression may be extreme.

The contrary is seen also. Probably pressure on the trachea alone produces this sensation. No parallelism exists between the degree of compression and the size of the heart. Therefore, the theory of the mechanical "Kropfherz" must be rejected and only the toxic "Kropfherz" seems to exist. Generally the left heart and often the right heart is enlarged. An isolated enlargement of the right heart, however, is very rare. The cardiac symptoms usually disappear rapidly after removal of the goiter. Improvement of the heart is not so marked if the goiter is not completely removed. Especially in very toxic goiters, as in Graves' disease, the quantity of thyroid left behind must be as small as possible. All forms of "Kropfherz" are different stages of the same disease. Therefore, the well-known classification, Rose's Kropfherz, Kraus' Kropfherz, and the "Kropfherz" in Graves' disease cannot be maintained. The author examined the heart of his patients some time after the operation. In some patients in whom the piece of thyroid removed was as large as possible some symptoms, especially palpitations, did not entirely disappear. This proves that the thyroid is not always the only seat of pathological changes in Graves' disease. Probably the abnormal constitution, which according to Chvostek is always present in Graves' disease, causes those symptoms of the heart which do not disappear after extensive surgical treatment.—J. K.

The value of basal metabolism determinations in the diagnosis and treatment of HYPERTHYROIDISM. Stoll (H. F.), Boston M. & S. J., 1922, **187**, 127-133.

The author emphasizes the value of this procedure in conjunction with other clinical methods and in determining the type of treatment to be used in hyperthyroid cases. He illustrates his points with case reports.—J. C. D.

(THYROID) Studies in the adaptation of albino mice to an artificially produced tropical climate. IV. Effect of light and heat on the resistance of mice to acetonitrile. Sundstroem (E. S.), Am. J. Physiol. (Balt.), 1922, **60**, 435-442.

In this paper acetonitrile is taken as an empirical test of thyroid activity and it is found that the resistance of mice is not augmented in humid heat. It is suggested that the tropical climate may lessen the demand for thyroid hormones in the body. The retardation of growth that occurs in humid heat is not attributable to a stimulation of thyroid activity. The resistance of mice exposed to strong light at ordinary room temperature is slightly diminished.—T. C. B.

(THYROID) Goiter. Reports of examination of 1,425 students. Taylor (J. G.), Wisconsin M. J. (Milwaukee), 1922, **21**, 181 (October).

All the 1,425 students examined by Taylor were girls ranging in age from 12 to 22 years. Tremor and tachycardia were present in 27% of the cases; exophthalmus in 0.8%. The right lobe was involved in 7.7%; the left lobe in 2.8%; the isthmus in 52%, and the whole gland in 40%. Of the students coming from Wisconsin 37% had enlarged thyroid. Among students coming from other states the incidence was, Missouri, 36%; Michigan, 34%; Minnesota, 32%; Indiana and Illinois, 30%; Iowa, 27%; Arizona and Nebraska, 25%; Ohio, 22%; South Dakota, 20%; North Dakota, 17%; Tennessee, 12%; Mississippi and Montana, 10%; Pennsylvania, 8%, and Colorado, 7%. None of the students from Kentucky, Texas, Kansas, New Hampshire, Alabama, Massachusetts or New Mexico presented any evidence of thyroid enlargement.—J. Am. M. Ass., **79**, 1880.

(THYROID) Congenital goiter (Kongenitale Struma). Treplin, Klin. Wchnschr. (Berl.), 1922, **1**, 1388.

The patient was an infant of 5 months. Respiration and swallowing were difficult. Histological examination showed the subject to have Graves' disease.—J. K.

(THYROID) A case of myxedema. Urban, Wien. klin. Wchnschr., 1922, **35**, 851.

A case of infantile myxedema, improved after implantation of thyroid. No details are given.—J. K.

Inflammation of the THYROID following parturition (Un cas d'inflammation du corps thyroïde dans les suites des couches). Valois & Roume, Gynéc. (Par.), 1922, **21**, 549.

Report of a primapara of 26 years having a mild goiter. She showed signs of intense congestion and inflammation of the thyroid on the 15th day after parturition. There was resolution without suppuration. The thyroid remained slightly larger than before the disturbance.—F. S. H.

(THYROID) Graves' disease after labor (Syndrome de Basedow apparu dans les suites de couches). Vermelin (H.), Bull. Soc. d' obst. et de gynéc. (Par.), 1921, **20**, 159-161.

Report of a case in which hyperthyroid symptoms appeared shortly after labor in a previously normal primapara of 30. (Fruhinsholz, in the discussion, expressed a belief that the thyroid condition was present before pregnancy and that it was improved during the latter, the symptoms reappearing in the puerperium). The pulse was 100 during labor. On the twelfth day it reached 120, later remaining at from 120 to 130. The patient also developed definite bilateral exophthalmos, together with pronounced tremor. The duration of these symptoms is not stated.—E. N.

THYROID and pregnancy (Corpo tiroide e gestazione). Vignes (E.), Med. prat. (Napoli), 1922, **7**, 281-289.

A review. The author deduces that one of the functions of the thyroid is to insure oval nidation.—G. C.

THYROID action and fever. Ward (E. H. P.), Med. Rec. (N. Y.), 1921, **100**, 399-407 (September).

The author states that the various actions of the thyroid secretion oppose those of **adrenalin**, and that the thyroid is responsible for rise of temperature in disease and the maintenance of normal temperature in health. The features of fever—throat vasodilation, full pulse, tachycardia, low blood pressure, headache, etc.—are all found to be in hyperthyroidism. Fever, therefore, is a manifestation of disturbance of balance between thyroid and adrenals.

—Prescriber, **16**, 357.

(THYROID) Stridor caused by goiter (Ueber den Kropfstridor). Wiltschke (F.), Wien. klin. Wchnschr., 1922, **35**, 726.

Description of 4 infants in whom oppressed respiration was caused by a goiter. Best results were obtained by administration of small quantities of NaI.—J. K.

(THYROID) The dosage and technique in the x-ray treatment of goiter, tuberculous glands of the neck, tonsils and adenoids. Witherbee (W. D.), Am. J. Roentgenol. (N. Y.), 1922, **9**, 514-516.

The author points out the association of infected tonsils, tuberculosis of the lungs and enlargement of the thyroid gland. He describes his treatment of these different conditions. His technique is as follows. Seven inch spark gap, 5 ma, 10 in. distance, 4 minutes time, filtered through 3 mm. of aluminum. The area of exposure for treatment of the thyroid extends from just above the external auditory meatus down to the lower level of the thyroid gland and transversely to the center of the middle lobe. Each side is given a four minute exposure, thereby including the tonsils and adenoids in a cross fire. The number of treatments is governed by basal metabolism determinations. The author has seen very favorable results, particularly in cases with infected tonsils. In no case was there evidence of impairment of the function of the thyroid or parathyroids.—J. C. D.

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